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Relationship between chromatographic retention and donor and acceptor numbers

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RELATIONSHIP BETWEEN CHROMATOGRAPHIC RETENTION AND DONOR AND ACCEPTOR NUMBERS

by

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ABSTRACT

The prediction of chromatographic retention times for a wide range of chemical compounds has been a subject of interest and intense study during the past few decades. Several of these studies are discussed, in particular those which utilize empirical parameters of solvent polarity in a correlation to chromatographic retention. Several of these empirical scales of solvent polarity are discussed in detail. The compilation of accurate acceptor and donor numbers is thoroughly discussed.

Correlation of some of these empirical parameters to the solvent's normal phase liquid chromatographic retention was attempted. The multiple variable correlation equation which resulted in the best correlation utilized the solvent analyte's acceptor number, donor number, and π^* value.

The gas chromatographic retention behavior of a wide range of solvent classes was also correlated to solvent property data. The highest correlation of this retention data was achieved using a multiple variable correlation equation involving the solvent's boiling point, donor number, and π^* value. In addition to these most successful attempts several other correlation equations are discussed.

1.0 INTRODUCTION

The measurement of solvent polarity is a subject that is of great interest and importance. Polarity is the term that describes the many possible solvent interaction mechanisms including those due to : acidic or basic functional groups, polarizable electrons, and dipole moments. Numerous measurement techniques have been utilized in determining these parameters. Chromatographic retention studies have been particularly prominent in gaining knowledge of the various interactions which occur in different solvents. These types of studies, which relate the structure of solutes to their chromatographic retention, are important also in explaining the mechanism of chromatographic separation as well as allowing for the prediction of retention coefficients. Several of these studies will be discussed in detail.

In this research project a solvent's Lewis acid-base characteristics, as quantified by donor and acceptor numbers, are used to determine the relationship between these solvent describing values and the solvent's chromatographic retention. Several empirical parameters of solvent polarity will be discussed after a brief introduction to early studies involving the application of solvent polarity to chromatography.

Some of the most important chromatographic studies done which provided a quantitative scale of solvent polarity are those performed by Lloyd Snyder.(1) The values obtained for the scale that Snyder tabulated were calculated from original experimental data collected by Lutz Rohrschneider in one of the preliminary studies of its type in 1973.(2)

In Rohrschneider's study 80 common solvents were characterized using gas-liquid partition coefficients determined by gas chromatographic headspace analysis. GC headspace analysis is a method that employs sampling of a solvent in its gaseous phase which exists in the headspace of the liquid solvent in an enclosed container. Acting as stationary phase liquids, six test solutes were chosen to represent the corresponding functional group classes: n-octane (paraffins), toluene (aromatics), ethanol (alcohols), methyl ethyl ketone (carbonyl compounds), dioxane (ethers), and nitromethane (nitro compounds). Due to the volatility of these solvents the six test solvents could not actually be used as stationary phase liquids. It is for this reason that a concentration study, relating to gas chromatographic retention, was done by determining the partition coefficients for the six test solvents with the 80 studied solvents. The relative solubility of the solvents were then determined from this partition coefficient data and correlated to previously gathered

solvent data such as the Hildebrand solubility parameter δ. However, this data was difficult to use and didn't fully characterize solvents. For these reasons Snyder expanded upon this data and was able to arrive at a scale of polarity indices (P') which describes a solvent's strength.

P' encompasses the proton-donor, proton-acceptor, and strong dipole interactions present in a solvent. The values of P' range from 0 for the most nonpolar solvents to 10.2 for the most polar solvent, water. This data is useful in describing solvents as mobile phases as used in Liquid-Solid (Adsorption) Chromatography and on their ability to selectively elute various other solvents based on their mutual interactions.

Solubility parameter theory has been used to explain retention in terms of the relative solubility parameters of the solute, mobile phase, and stationary phase. However, it is impossible to measure the solubility parameter of the stationary phase in a LC system. Therefore, these methods do not take into account the solvent's individual interactions with the stationary phase.(3)

Empirical parameters were developed in order to more accurately quantify solvent polarity as a function of the individual interactions that occur. Several scales have been developed and will be discussed in detail in the following sections.

1.1 EMPIRICAL PARAMETERS OF SOLVENT POLARITY

Empirical parameters of solvent polarity provide a more comprehensive measure of the overall solvation ability of the solvents than do their individual physical data such as the dielectric constant or the permanent dipole moment. In this sense the term "solvent polarity" is understood as the overall solvation ability of a solvent. This overall effect is therefore dependent upon all of the possible specific and non-specific intermolecular forces between solute and solvent molecules. An example of a non-specific force is that of the London dispersion interactions. Specific forces include the hydrogen-bond donor-acceptor, electron-pair donor-acceptor, and solvophobic interactions (4). Due to the great number of interactions one physical parameter could not be used to fully describe a solvent's polarity. This led to the introduction of empirical parameters of solvent polarity.

In order to determine an empirical solvent parameter one first views the solvent effect on a chosen standard process. The solvent influence can then be determined for a series of other reactions or absorptions correlating with this empirical parameter.

One of the most prevalent methods for the calculation of empirical parameters of solvent polarity is the solvatochromic method. Solvatochromism involves the

observation of the change in the position of an absorption band of a molecule as a fuction of the solvent (5). A solvatochromic study is done by measuring the absorption maxima for an indicator compound (dye) present in the solvents of interest. Although solvatochromism has been used most frequently, other methods are employed in the determination of empirical parameters. In many cases, several different methods may be used to evaluate the empirical parameters for a given solvent.

In this study the empirical parameters of main concern are the donor and acceptor numbers. It was theorized that these parameters would be able to cover all interactions. The acceptor number represents the solvent's ability to accept a pair of electrons. The donor number represents the solvent's ability to donate a pair of electrons. This concept is a restatement of the generalized Lewis acid-base definition. Lewis acid-base theory defines an acid as an electron pair acceptor and a base as an electron pair donor. Therefore, the interactions which occur between solvents can be described as Lewis acid-base interactions. With values of DN and AN one may quantitatively predict the strength of these interactions.

DN and AN determinations will be discussed in detail in later sections. Prior to this, two important solvatochromic parameters, $E_T(30)$ and π^* will be discussed

1.1.1 $E_T(30)$ SCALE

The largest scale of solvent polarity that was determined by the solvatochromic method is the $E_T(30)$ scale. The $E_T(30)$ parameter is defined as the molar transition energy (kcal/mole) measured for the $\pi - \pi^*$ absorption of 2,6-diphenyl-4(2,4,6-triphenyl-1-pyridinio) phenolate (the standard probe). The $E_T(30)$ scale is the most comprehensive solvent scale due to the number of interaction sites present on the probe (Figure 1).

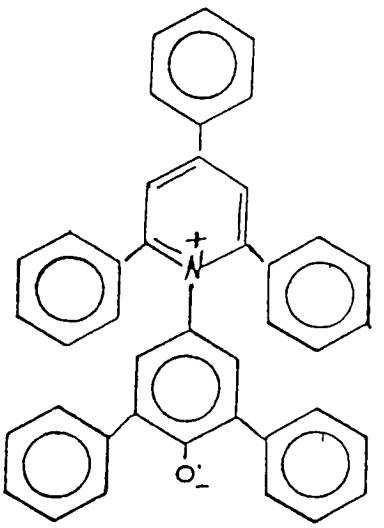

Figure 1. 2,6-diphenyl-4(2,4,6-triphenyl-1-pyridinio) phenolate

The possibility exists for hydrogen bonding at the phenoxide site, dipolar interactions with the N - O dipole, and dispersion interactions with the large polarizable π- electron system from the aromatic rings (6).

Different solvents will produce varied interactions which will induce different solvatochromic intramolecular charge-transfer absorptions in the dye. This transition energy measured for each solvent in kcal/mole is strictly defined as the $E_T(30)$ value. High $E_T(30)$ values correspond to solvents of high polarity.

It has become apparent that the utilization of one parameter for the measurement of all interactions of all classes of solvents is not possible. Hence different scales are more suited to the measurement of the interactions of certain solvent classes. Another solvatochromic parameter which provides a better measure of the interactions of nonpolar solvents is the π^* scale.

1.1.2 π^* SCALE

The solvatochromic parameter π^* provides an accurate measure of a solvent's ability to interact through dipolar or dispersion interactions. These are the prominent interactions which occur in nonpolar solvents. Since nonpolar solvents are studied extensively in this project, this parameter is used to describe the contributing interactions which occur. The π^* scale is used to describe the solvent's ability to stabilize a charge or a dipole through its dielectric effect. The π^* scale is so named because it derives from solvatochromic effects on p --> π and π --> π^* electronic spectral transitions (7). In these measurements solvent effects on π^* values of several indicator compounds (dyes) are utilized in the initial compilations of the scale. The important concept that was considered in choosing the indicator compounds was that the method should exclude or at least minimize hydrogen bonding effects in determining π^* values for hydrogen donor - acceptor solvents. The indicator compounds chosen were comprised of various substituted nitro-aromatics due to their high degree of dipolarity (7).

In a related study the π^* parameter was compared to the Hildebrand solubility parameter δ (8). This study revealed a rather poor correlation between these two

scales. It was reasoned that based on the methods of determination the π^* parameter is a better measure of the ability of the solvent to stabilize a dipolar or charged solute through solvent dipole / solute charge or solvent dipole / solute dipole interactions. δ is a better measure of solvent dipole / solvent dipole interactions (8).

This was an important study in that it established that the applicability of a scale is based on its methods and indicators of determination. In this case, δ was developed by measuring the changes which occur between two solvent molecules, and is therefore a better measure of solvent / solvent interactions. π^* was developed by measuring the changes that occur between indicator solutes and solvents of interest, and is therefore a better measure of solvent / solute interactions. This study revealed that free energies of solution (ΔG) are best correlated with both the δ and π^* in multiple parameter regression equations.

1.1.3 DONOR NUMBER SCALE

The donor number (DN) scale of solvent polarity was originally devised and compiled by Victor Gutmann (9). Gutmann utilized a calorimetric method to make measurements of the enthalpies of reaction for each of the solvents studied with the strong Lewis acid (electron pair acceptor) $SbCl_5$. The reactions were carried out in dilute 1,2-dichloroethane in order to reduce the electrostatic contributions. Equation 1 shows the interaction of the Lewis basic solvent B: with the antimony pentachloride.

$$B: \; + \; SbCl_5 \xrightarrow{CH_2ClCH_2Cl} B{-}{-}SbCl_5 \qquad [1]$$

$$DN = -\Delta H_{rxn} \text{ (kcal/mole)}$$

From these measurements Gutmann obtained donor numbers for 53 solvents.

Due to the fact that Gutmann obtained DN data for such a limited number of solvents several other empirical scales were correlated with the DN scale. These parameters are: $\Delta\tilde{\nu}_D$, D[II,I], β, B, and $-\Delta H(BF_3)$. Their determinations will be described in detail later in this section. For this project these correlations were done for two main reasons. First, the values of DN from the various scales may be averaged to increase the

reliability of the donor numbers calculated. Secondly, the number of solvents for which DN data is available can be greatly augmented by combining the lists. Several of these related scales will be discussed at this point.

Maria and Gal proposed another calorimetrically determined measure of solvent polarity (10). The $-\Delta H(BF_3)$ scale is defined as the enthalpy change for the reaction of gaseous boron trifluoride and the basic organic solvents of interest. In this study they also discuss the failings of the donor numbers as determined by Gutmann.

The main criticism of the DN scale was that Gutmann's enthalpy measurements were erroneously determined for some selected solvents. Maria and Gal showed that the DN scale is not always reliable, due mainly to experimental problems. These problems include inappropriate reference solvents, Lewis acid reactivities, and the inaccuracies associated with the outdated calorimetric method used by Gutmann. For example the donor numbers for weak bases given by Gutmann were underevaluated because no correction was made to take complex dissociation into account (10). Through inspection of trends within a class other evaluations which are specific to individual solvents were found to be in error.

Maria and Gal stated that their scale $-\Delta H(BF_3)$ much more accurately described the basicity of a solvent.

In their original experimental method accurate measurements of enthalpies of reaction were obtained. This was because this method allowed for the detection of possible side reactions and also because the stoichiometry of the complex reaction was controlled. Neither of these were considered in Gutmann's scale of donor numbers. The relationship between $-\Delta H(BF_3)$ and $-\Delta H(SbCl_5)$ for a series of solvents is presented in Figure 2. A better fit was expected due to the similar strengths and steric requirements of BF_3 and $SbCl_5$. It is from these deviations from 100% linear correlation that Maria and Gal were led to believe that Gutmann's DN values were erroneous. Nevertheless, in light of the open nature of these types of correlations, the relationship between $-\Delta H(BF_3)$ and DN is considered to be very good and values of $-\Delta H(BF_3)$ correlate well to donor numbers and are therefore used as an additional way to calculate DN values. The relationship between these two scales is given by equation 2 which was determined by least squares analyses of the correlating data.

$$DN = \frac{1.09\ (-\Delta H(BF_3)) - 4.83}{4.184} \qquad [2]$$

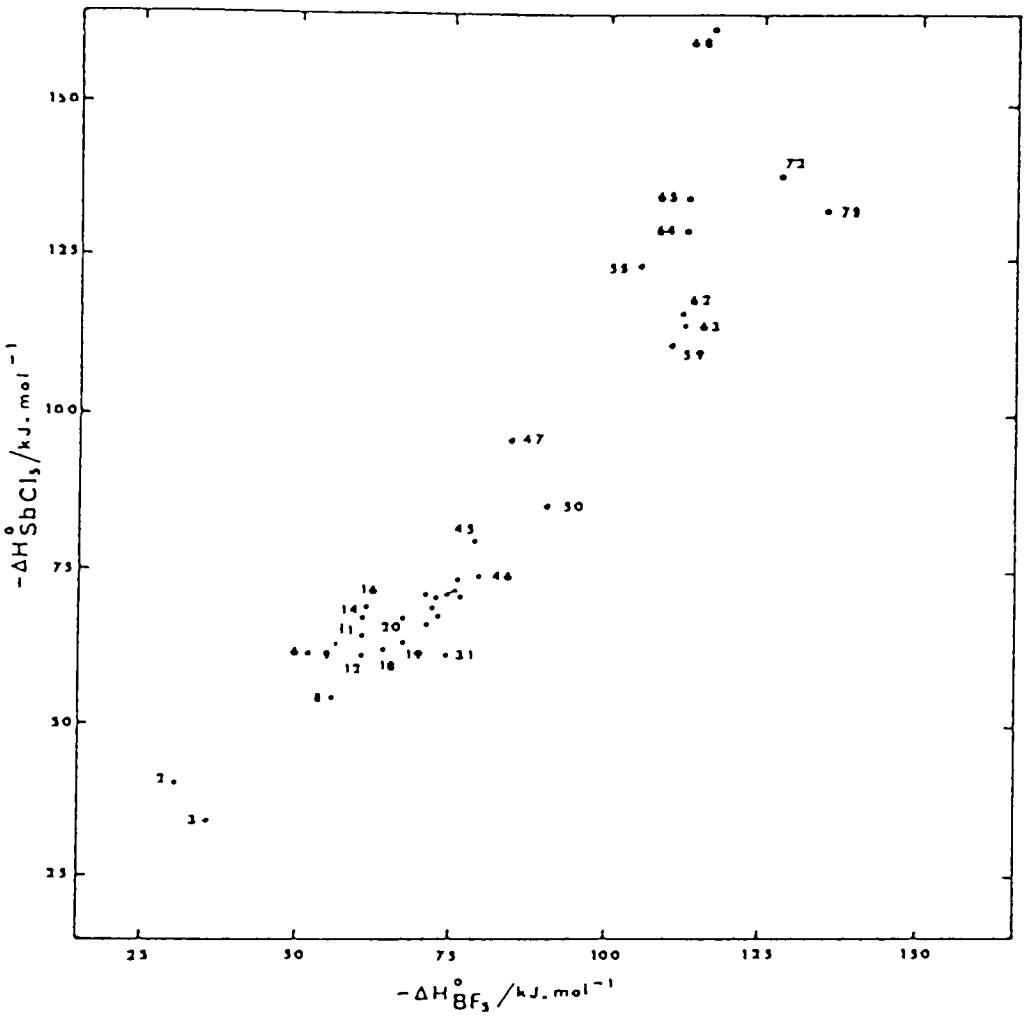

Figure 2. Plot of $-\Delta H(SbCl_5)$ vs. $-\Delta H(BF_3)$ for a variety of solvent classes (10). Correlation coefficient (R^2) is .963. Data used to calculate Equation 2.

Another scale that correlates very well with donor number is the spectroscopic scale $\Delta\tilde{\nu}_D$. This relationship is discussed in detail in a paper by Griffiths and Pugh (11). These frequency shift values were obtained by Kayiga et al. in a quantitative study of the electron-donating nature of organic solvents using infrared spectroscopic techniques of the donating power of a solvent. The donating powers were compared by measurement of the change induced on the O-D vibrational band of methanol-d or the C=O vibrational band of acetophenone. It is defined as the relative difference, in wavenumbers, of the O-D or C=O absorption frequency absorbed in the solvent from that in benzene. The equation for this is:

$$\Delta\tilde{\nu}_D = \Delta\tilde{\nu}(\text{benzene}) - \Delta\tilde{\nu}(\text{solvent}) \qquad [3]$$

The relationship between DN and the $\Delta\tilde{\nu}_D$ values for a series of solvents is given in Figure 3.

As derived from regression analysis of the above data the correlation equation which relates the two is given by equation 4.

$$DN = .20\ (\Delta\tilde{\nu}_D) + 3.03 \qquad [4]$$

Selbin and Ortolano devised a scale in which they estimated the degree of interaction between various solvents and $[\ VO(acac)_2]$ by studying the resulting

electronic spectra. In this region two band-shifts were used, band I which moves to higher energies, and band II which goes to lower energies. The degree of interaction of the donor solvent with $VO(acac)_2$ is estimated from the energy difference, D(II,I). Figure 4 shows a plot of DN vs. D(II,I) for various solvents.

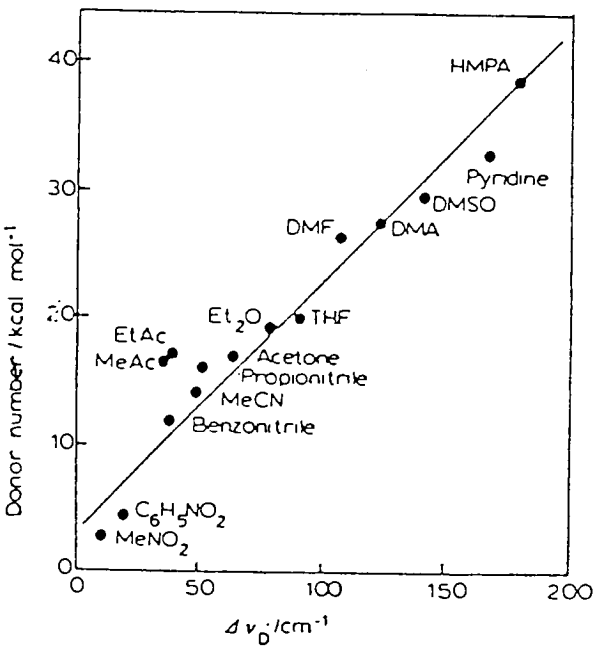

Figure 3. Correlation between donor numbers and $\Delta\nu_D$ values (11). Data used to calculate Equation 4.

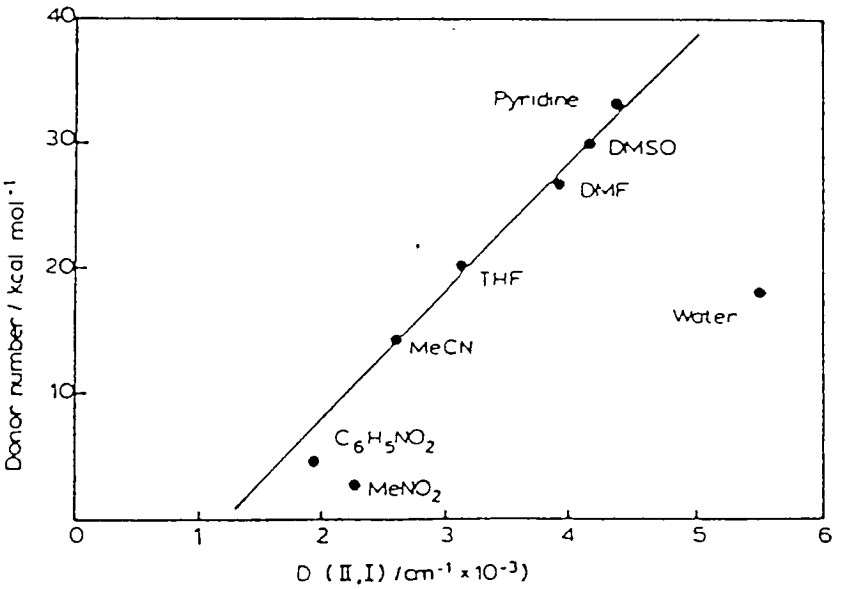

Figure 4. Correlation between donor numbers and D(II,I) values (11).Data used to calculate Equation 5.

From a least squares regression analysis of this data equation 5 was derived giving the relationship between D(II,I) and DN.

$$DN = 10.11\ (D(II,I)) - 12.17 \qquad [5]$$

The β scale of solvent hydrogen bond acceptor basicity was created by another application of the solvatochromic comparison method. In this method uV spectral shifts are measured in the various solvents under study for 4-nitroaniline and compared to the shift produced by the corresponding solvents on N,N-diethyl-4-nitroaniline (12).

In order to correctly determine solvent-solute hydrogen bonding interaction by this method it was concluded that several criteria be met. The first condition which was fulfilled was that a plot of corresponding ν_{max} values for two solutes of hydrogen bonding ability (4-nitroaniline and N,N-diethyl-4-nitroaniline) in a series of non-hydrogen bonding solvents gives a linear relationship. The second condition was that hydrogen bonding solvents should deviate from the regression line by statistically significant amounts. Finally, these deviations should be indicative of the magnitude of the solvent's hydrogen bond donor strength. All of these conditions were met in this study with very good correlation coefficients (R^2

greater than .95) being obtained for the equations used. The plot of DN versus β appears in Figure 5 . The resultant β values were found to relate very well to DN through equation 6 .

$$DN = 38.4 (\beta) - .78 \qquad [6]$$

Finally, another empirical parameter used to calculate donor numbers is the Lewis basicity parameter, B. This relationship was suggested by Schmid (13). This scale was determined in a manner similar to the β scale except with different spectral probes. The B scale is based on the wave number differences in the IR stretching absorbance of O-D in CH OD in the presence of the solvent of interest. A plot of B vs. DN is given in Figure 6 . Through linear regression analysis of this data equation 7 was arrived at which relates B to DN.

$$DN = -6.36 + .19 B \qquad [7]$$

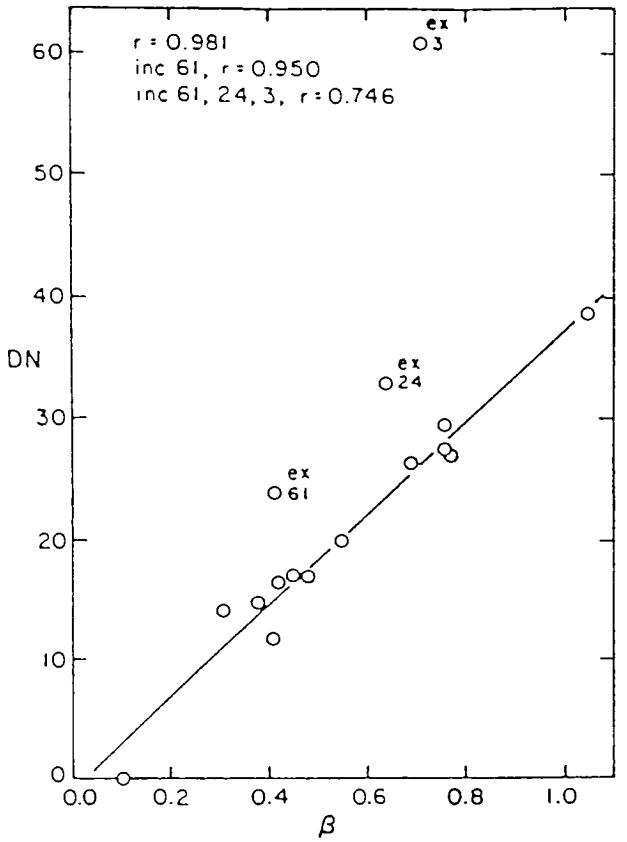

Figure 5. DN plotted vs. β for various solvents (12). Used in calculation of Equation 6.

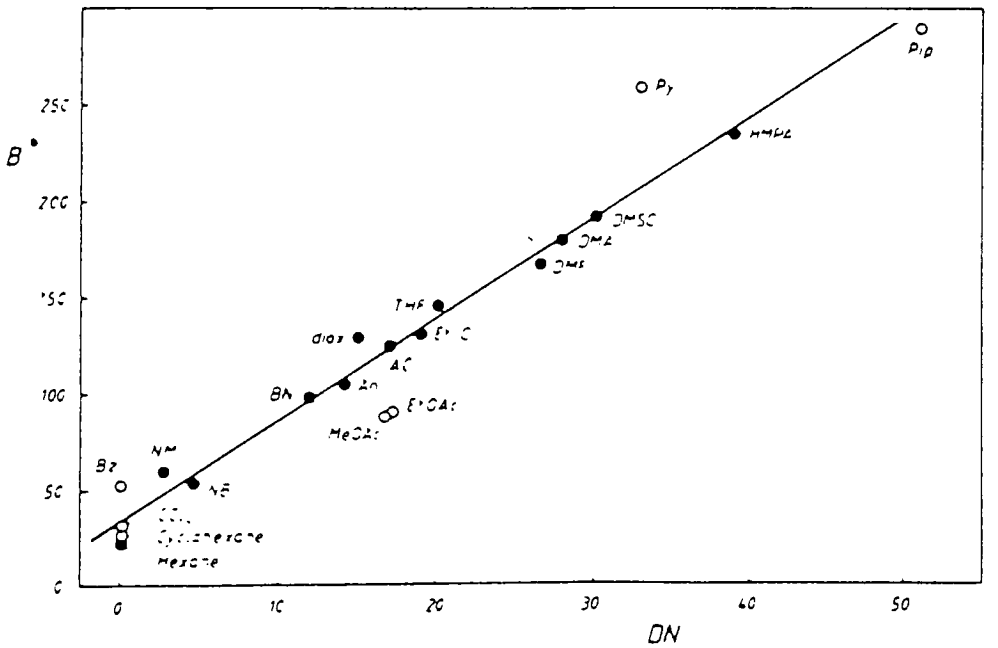

Figure 6. Lewis basicity parameter B vs. DN (13). Used to calculate equation 7.

1.1.4 ACCEPTOR NUMBER SCALE

The acceptor number (AN) is defined as the P^{31} nmr chemical shift observed for the reference base $(C_2H_5)_3$ PO when dissolved in the solvent in question. This reaction given by equation 8 shows the interaction which occurs between the Lewis acidic solvent (A) and the standard probe triethylphosphine oxide (13).

$$(CH_3CH_2)_3P\text{-}O: + A \longrightarrow (CH_3CH_2)_3P\text{-}O\text{-}A \qquad [8]$$

The values of AN are defined relative to n-hexane which has an AN equal to zero and antimony pentachloride which has an AN of 100. In this particular group of solvents, hexane is the least electron accepting solvent and antimony pentachloride the most electron accepting solvent. The nmr shift measured in ppm induced by the solvent on the standard probe triethylphosphine oxide is given relative to these as shown by equation 9.

$$AN = 100 \frac{\delta(Et_3PO\text{-}A) - \delta(Et_3PO\text{-}Hexane)}{\delta(Et_3PO\text{-}SbCl_5) - \delta(Et_3PO\text{-}Hexane)} \qquad [9]$$

Acceptor numbers were determined by this method for 34 solvents. In order to augment the list of solvents for which AN data is available the $E_T(30)$ scale of Lewis acidity was utilized in a correlation to AN.

In a study relating the various available empirical scales of solvent polarity to one another Reichardt derived equation 10 from the linear regression analysis of the AN vs. $E_T(30)$ data for 38 solvents (Figure 7).

$$AN = 1.598\ (E_T(30)) - 50.69 \qquad [10]$$

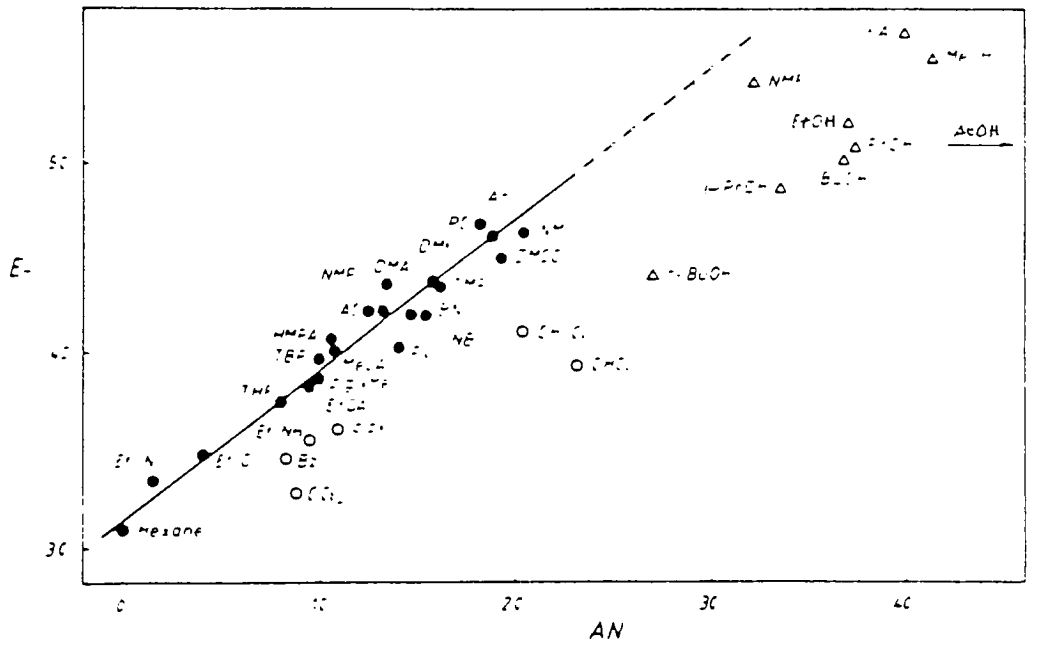

Figure 7. Relationship between E_T values and AN (13). Data points in full circles are used to calculate Equation 10.

The highly structured solvents: alcohols, acids, and chlorinated hydrocarbons deviated from this equation and were therefore excluded from consideration in calculating equation 10.

Schmid found a similar correlation equation relating $E_T(30)$ with AN also to the exclusion of the structured solvents mentioned(13). In this same study Schmid also determined a correlation of AN and DN with the dielectric constant, ε :

$$\log \varepsilon = .071\ (AN) + .0054\ (DN) + .258 \qquad [11]$$

Therefore given two of the three variables for a given solvent the third may be calculated. A more detailed discussion of the determinations of AN is given in the thesis of Lan Evans (25).

1.2 CHROMATOGRAPHIC INTERACTIONS

1.2.1 LIQUID CHROMATOGRAPHY

In order to be able to accurately predict retention times for a wide range of sample solvents a good understanding of the mechanism of retention is required. In this study the LC method utilized is that of liquid-solid (adsorption) chromatography. The solid adsorbant used throughout is a silica gel packing. Due to the fact that the mobile phase used is the inert n-hexane all prominent, retention-causing interactions will be those which occur between the silica and the solute (here, the numerous solvents of interest).

The mechanism for adsorption is quite simple. As the sample moves through the adsorbent bed, its various components will be held (adsorbed) at the adsorbent surface to a greater or lesser extent, depending upon the chemical nature of the component (14). An illustration of the silica surface with its active hydroxyl sites located as indicated is given by:

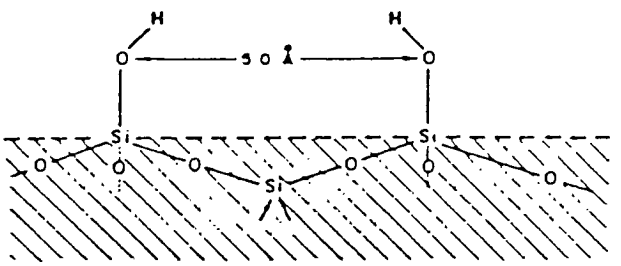

Figure 8. Silica gel surface (14).

The surface of a crystalline silica consists of a plane of exposed silicon atoms which are covalently bonded to hydroxyl groups. These sites along with their positioning are the source of the selective adsorption of many molecules. The active sites interact with these adsorbed molecules by hydrogen bonding with the adsorbate molecule which functions as an electron donor. It has been determined that by increasing the basicity of an adsorbate molecule its adsorption energy on the silica increases which implies acidic surface sites (15).

Previous studies of empirical parameters in the prediction of retention in LC utilized Reversed-Phase chromatography. A brief description of this form of LC will therefore be given here. Reversed-phase liquid chromatography is a very popular type of liquid-liquid chromatography and has been studied extensively over the past several years. Reversed-phase LC utilizes a nonpolar hydrocarbon (usually C8 or C18) bonded phase chemically attached to a solid packing material such as silica gel. The mobile phase is usually an aqueous based solvent mixture, the most commonly used mixtures are methanol/water or acetonitrile/water. The role of the organic modifiers is to selectively interact with solutes of different funtionalities. Increasing the amount of the organic modifier increases the strength of the mobile phase. A stronger mobile phase in RPLC provides a more nonpolar solvent mixture which interacts stronger with

the nonpolar analytes.

There have been several theories of retention mechanism proposed. The most widely accepted mechanism is that described by Horvath and Melander (16). They stated that retention in reversed-phase LC is based upon the hydrophobic interactions which occur in the process of retention. The water from the mobile phase is so strongly self-interacting that in order for the solute to be dissolved, water's network structure must be distorted so that nonpolar solutes are "squeezed out" of the mobile phase and bind to the hydrocarbon ligands of the stationary phase. In this sense the driving force for retention is seen as the effect of the solvent in pushing the solute onto the hydrocarbon stationary phase. Selectivity in this theory is shown to arise from size differentiations among the solutes and in their areas in which favorable nonpolar attractions are achieved with the hydrocarbon ligands of the stationary phase (17).

1.2.2 GAS CHROMATOGRAPHY

Capillary gas chromatography is also utilized in this project in correlation of empirical solvent polarity data to retention. Gas-liquid chromatography accomplishes separation by partitioning solutes between a mobile gas phase and a stationary liquid phase. The stationary liquid phase, which provides the separation of the sample, is coated onto the inside of the column in an open-tubular capillary column. The relative solubility or retention of different compounds in the stationary phase liquid is based on solvent volatility and is controlled primarily by column temperature. An increase in temperature results in decreasing retention for all sample components. This phenomenon is understood through temperature's relationship to the partition equilibrium constant, K. The following thermodynamic equilibrium equation shows this inverse relationship.

$$\ln K = \frac{-\Delta G}{RT}$$

where R is the gas constant and ΔG is the free - energy change associated with the retention process.

In this project a nonpolar stationary phase is utilized. Nonpolar stationary phases are generally non-selective, meaning that the volatility of the solute is primarily determined by its vapor pressure. Therefore

retention will be in the order of increasing boiling points of the solutes. Separation of compounds of similar volatility is effected through the differences in the partition coefficients of the materials (18). Stated more simply the degree of retention depends upon the tendency of the solvent analyte to dissolve in the stationary phase.

1.3 LINEAR REGRESSION ANALYSES

Though similar in concept and closely related the terms correlation and regression are different. Correlation is the most common measure of the association between two variables x and y. Regression takes this further. Regression analysis gives an equation that can be used to predict one variable from the other (19). The following will serve to describe various aspects of regression analysis.

The simplest type of linear function is of the form: $y = mx + b$. Where x is a property which exerts an influence on the y term. From a plot of y vs. x a straight-line relationship would provide the slope (m) and the y-intercept (b). To determine the best straight line which fits through a given set of experimental data a least squares analysis is performed. The method of least squares assumes that the errors in the y values are greater than the errors in the x values and that the deviations in all of the y values are similar. The vertical scale's deviations are minimized and the squares of these are taken. This corresponds to assuming that the set of y values is the most probable set. Thus the choice of slope and y-intercept is based upon the minimization of the sum of the squares of the vertical deviations (20). Obviously least squares analyses are only as reliable as the reliabilty of the y axis values.

In order to test the significance of the observed relationship in a linear regression analysis several statistical tests can be performed. One of the most important characteristics of a statistical fit is the R^2 statistic. R^2 is defined in terms of the sum of the squares of deviation about the mean SS(mean) and the sum of the squares of deviation due to error SS(error). The better a set of data fits a line the lower SS(error) becomes. The R^2 statistic utilizes this property and is calculated through the equation:

$$R^2 = \frac{SS(mean) - SS(error)}{SS(mean)} \qquad [12]$$

Thus the best value of R^2 is 1.0 which indicates 100% data correlation. For example using the $y = mx + b$ relation an R^2 value of 1.0 would mean that 100% of the variation in y is explained by variation of x.

Another statistical method for analyzing data is the overall variance ratio, F. This is an important statistical tool because it is dependent upon the number of data points and not just on the fit of the available data. It is used to assess the statistical significance of the observed regression and may be calculated from an ANOVA (Analysis of Variance) table. Table 1 represents a generalized ANOVA table for a simple one variable regression (21).

Table 1. Simple Regression ANOVA Table

Source of Variation	SS	Degrees of Freedom	Mean Square (MS)
Regression	$\Sigma(\hat{Y} - \bar{Y})$	1	$\frac{\Sigma(\hat{Y} - \bar{Y})}{1} = MS(reg)$
Error	$\Sigma(Y - \hat{Y})$	n-2	$\frac{s^2}{n-2} = MS(error)$
Total	$\Sigma(Y - \bar{Y})$	n-1	

SS is the sum of the squares of the deviations in the y-axis terms. The degrees of freedom are directly related to the population size, n. MS is the mean square term which describes the deviations from the mean.

The F ratio is related to R by the relationship:

$$F = (n-2)\frac{R^2}{(1-R^2)} \qquad [13]$$

where n-2 represents the number of degrees of freedom. F is also defined as:

$$F = \frac{MS(reg)}{MS(error)} \qquad [14]$$

The above parameters may be obtained from the ANOVA table. Todays modern statistical computer programs will provide an analysis of variance table which gives a

breakdown of the variation in the data.

In more complex regression analyses two or more variables are used in the prediction of another. The best and most realistic way to do multiple regression calculations is through use of a computer. The goal in studying these relationships is to calculate the best least squares equation for all the data while determining the statistical significance of the contribution of each of the predictor variables. The coefficients of the parameters in the multiple regression equation are determined in the same way as they are in a simple least squares analysis. The only difference is that in a multiple regression analysis the slope and the x variable term refer to a list of predictor values rather than one value (21). The nature of the resulting multiple variable equation is higher in dimension than a simple linear regression equation. Therefore, it cannot be described in one plane. The R^2 and overall variance ratio, F, are likewise determined in a manner similar to the way in which they are determined in simple least squares analyses.

1.4 EMPIRICAL EQUATIONS DESCRIBING SOLVENT EFFECTS

1.4.1 GENERAL EQUATION

In recent years numerous studies have been performed in which solvent effects have been related to empirical parameters. In this introduction, initially general equations describing this relationship are discussed. Later in this section, more specific and relevant chromatographic relationships are described.

A study by Krygowski and Fawcett provides a general theory which describes solvent effects on physical and chemical (physicochemical) properties measured in solution (22). They concluded that reliable predictions of solvent effects can be obtained from empirical relationships. The effect of the solvent on the quantity being measured, Q can be described by the linear relationship given by equation 15.

$$Q = \alpha P + \beta \qquad [15]$$

P is an empirical parameter which is used to indicate the contribution of the solvent's influence on the property Q. The constants α and β are derived from linear regression analysis.

More specifically, the purpose of the Krygowski and Fawcett study was to describe solvent effects showing that the influence of all solute-solvent interactions on

the different physical and chemical properties can be defined in terms of the solvent's Lewis acidity and basicity characteristics. The Dimroth - Reichardt E_T parameter (6) is used to describe the Lewis acidity of the solvent. Donor number (DN) is used to quantify the Lewis basicity characteristics of the solvent. Equation 16 shows this relationship.

$$Q = \alpha E_T + \beta DN + Q_o \qquad [16]$$

The constants and b provide information regarding the contributions of E and DN in describing Q. Q_o, α, and β are calculated from multiple linear regression analysis. Q_o is an intercept term which should equal Q when there are no Lewis acid or base effects influencing the property Q. Therefore, Q is best described as the sum of all the contributing interactions.

It is not possible to obtain a good quantitative measure of the relative importance of solvent acidity and basicity for a given physicochemical quantity just by examining the regression coefficients α and β. In order to determine the relative importance of the solvent parameters, the partial regression coefficients α' and β' are calculated. These coefficients are given in the following relationship by equations 17 and 18.

$$\alpha' = |\alpha| \left(\frac{\sum_{i=1}^{n} (E_{T_i} - \bar{E}_T)^2}{\sum_{i=1}^{n} (Q_i - \bar{Q})^2} \right)^{1/2} \qquad [17]$$

$$\beta' = |\beta| \left(\frac{\sum_{i=1}^{n} (DN_i - \overline{DN})^2}{\sum_{i=1}^{n} (Q_i - \bar{Q})^2} \right)^{1/2} \qquad [18]$$

E_{T_i}, Q_i, and DN_i are the values of E_T, DN, and Q for a given solvent and $\bar{E}_T$, $\overline{DN}$, and $\bar{Q}$ are the average values of these quantities for the given data set.

This type of data manipulation is done in order to determine actual percent contributions of each of the terms when scales of different magnitude are inter-correlated.

1.4.2 SPECIFIC APPLICATIONS OF EMPIRICAL EQUATIONS

In Krygowski and Fawcett's study several physical and chemical properties were correlated to E_T and DN using equation 16. One application they found was to the study of ^{23}Na NMR chemical shifts as a function of salt type and concentration as well as the nature of the solvent. It was determined that depending upon the type and concentration of the salt present a strong relationship existed between the NMR shift of the Na nuclei and the solvent's basicity and to a lesser degree the solvent's acidity. Very good correlation coefficients were obtained for various concentrations of $NaClO_4$ and $NaBPH_4$ solutions and evidence of the solvent's effect on the shift was shown.

Krygowski and Fawcett also found application for equation 16 in the study of solvent activity coefficients for several anions and cations. They determined that the solvent's acidity-basicity parameters are good measures of the enthalpy change associated with solute-solvent interactions. However, to a good approximation the E_T parameter was found to be able to correlate well with entropy changes so that α can be used to reflect the solvent's acidic interactions as well as solvent structure description. They found that the acidic properties of the solvent are important in anion stabilization and therefore the α term is large (greater

contribution) relative to the β term. Conversely, with cations the β term is found to contribute greatly in its correlation to the solvent activity coefficient.

Similar correlations using equation 16 were done with applications to enthalpies of ionic solvation and also to voltammetric studies of the standard reduction potentials of organic molecules.

1.4.3 CHROMATOGRAPHIC RETENTION STUDIES INVOLVING EMPIRICAL EQUATIONS

Some of the most recent developments in the study of empirical parameters of solvent polarity involve chromatographic retention studies. In recent years gas chromatographic and reversed-phase liquid chromatographic studies have been done relating retention to various solvent polarity measurements. Reversed-phase LC studies have utilized solvent polarity measurements for solvents as both mobile phases and as analytes (solutes).

In a study done in 1986 by Johnson et al. the $E_T(30)$ polarity values of binary solvent mobile phases were related to reversed-phase LC retention (5). Since binary solvent mobile phases are used extensively in reversed-phase HPLC the first thing that had to be done was to measure the $E_T(30)$ values of the solvent mixtures. Thus solvatochromic absorption shift measurements were obtained for various compositions of both methanol/water and acetonitrile/water binary mixtures.

Various compounds were used as solutes and retention measurements were obtained for each using different mobile phase compositions. Plots of log k' vs. E_T (30) values for the different mobile phases were done for each of the analyte compounds. Excellent correlation coefficients were obtained from the simple linear regression analyses. They determined that the slope and

the y-intercept were very much dependent upon the solute and solvent system. Solute size was also found to be a major contributor as evidenced by the fact that with increasing solute size both the slope and y-intercept increase. Thus solvatochromic solvent polarity measurements allow an independent examination of the effect of varying mobile phase polarity on chromatographic retention (5).

In an extremely different approach from that discussed previously Sadek et al. utilized solvatochromic polarity measurements of solvents as analytes in relation to chromatographic retention. The solute properties used in relating to reversed-phase LC retention are: molar volume or the cavity term ($\bar{V}$), hydrogen bond basicity (B) and solute dipolarity/polarizability (π^*). They report the first correlation of HPLC retention properties with fundamental dipolarity/polarizability and hydrogen bonding properties of the solutes and mobile phases.

Twenty nine organic solvents, comprised mainly of various substituted aromatics, were chromatographed using an octadecylsilane (C18) column and a 55/45 methanol/water mobile phase. Equation 19 resulted from the linear regression analysis of the solute properties with their reversed-phase retention behavior, as measured by the capacity factor, k'.

$$\log k' = (1.47)\bar{V}/100 - (.61)\pi^* - (1.97)\beta - .16 \qquad [19]$$

Equation 19 is in the form of the general expression equation 20.

$$\log k' = (m)\bar{V}/100 - (s)\pi^* - (b)\beta - SP_o \qquad [20]$$

Greater than 98% linear relationships were obtained for a variety of mobile phase compositions and for several different columns (stationary phases). Different values of m, b, s, and SP are obtained when using either a different mobile phase or a different stationary phase. Through inspection of equation 19 one can see that given that the parameters V/100, π^*, and β are of equivalent magnitude the greatest contributions are due to the solute volume term (V/100) and to the solvent basicity term (β), with a lesser contribution due to the solutes dipolar or polarizability interaction capabilities.

This was an important study in that it was the most successful reversed-phase liquid chromatographic study utilizing empirical parameters of solvent polarity for solutes in the prediction of their retention behavior.

The solvatochromic comparison method has also been used to explore the gas chromatographic retention of dipolar and nondipolar solutes on a series of similar polymeric stationary phases (24). The π^* scale of solvent polarity was used in this GC study to determine the polarity characteristics of the liquid siloxane polymers. They observed the presence of measurable hydrogen bond acceptance in these liquid polymers. This is of

importance due its potential applications to studying silica packing in liquid chromatography. The study showed that interactions of strong hydrogen bonding solutes with the siloxane backbone of silica gel packing in LC become a significantly important retention causing effect.

2.0 OBJECTIVES

The primary goal of this research project was to relate a solvent's Lewis acid-base characteristics to its chromatographic retention behavior. In order to achieve this goal it was first necessary to create complete lists of solvents with their corresponding donor and acceptor numbers. This is done through the compilation of literature values and also through calculations involving related parameters. Thus, more specifically, the goal is to determine if AN and DN values will be a useful tool in chromatography.

The chromatographic system used first is an adsorption system employing a silica gel stationary phase with a hexane mobile phase. It is necessary to have a minimum number of retention-causing interactions and with this liquid chromatographic system the only prominent interactions will be between the solvent and the stationary phase. Retention data for a series of solvents is then related to the solvent's polarity measures through an empirical equation derived through regression analysis. This equation could then be used in the prediction of retention times using only empirical solvent data.

Gas chromatographic retention studies are done using a nonpolar stationary phase to analyze polar solvents which couldn't be studied with the LC system

chosen. Regression analysis of the data would provide an equation allowing for the prediction of a solvent's gas chromatographic retention behavior.

3.0 EXPERIMENTAL

3.1 Materials

The following available solvents were distilled prior to use to ensure purity: acetophenone (Baker), aniline (Baker), benzene (Baker), 1-butanol (Baker), t-butanol (Baker), butyl ether (Fisher), chlorobenzene (Kodak), cyclohexanol (Fisher), N-methyl-2-pyrrolidone (Fisher), N,N-dimethylacetamide (Fisher), triethylamine (Kodak), dimethyl sulfoxide (Baker).

The following high purity solvents were also used: acetone (EM Science), benzaldehyde (Baker), benzonitrile (Fisher), benzyl alcohol (Fisher), bromobenzene (Kodak), carbon disulfide (Fisher), carbon tetrachloride (Fisher), chloroform (Fisher), cyclohexanone (Baker), o-dichlorobenzene (Kodak), dichloromethane (Kodak), 1,2-dimethoxyethane (Baker), ethyl acetate (Baker), ethyl benzoate (Fisher), ethyl ether (Fisher), ethyl formate (Fisher), fluorobenzene (Kodak), formamide (Aldrich), n-hexane (Baker), iodobenzene (Kodak), methyl ethyl ketone (Baker), nitroethane (Kodak), nitromethane (Kodak), nitrobenzene (Baker), pentane (Baker), 2-propanol (Baker), tetrahydrofuran (Baker), toluene (Baker), m-xylene (Kodak), o-xylene (Kodak).

3.2 Thin Layer Chromatography

Thin layer chromatographic studies were done using Eastman Kodak 13181 Silica Gel Chromagram Sheets with fluorescent indicator. Plates were activated in a 100°C oven for 15 minutes prior to use. The solvent used as eluent was spectral grade n-hexane. Thin layer chromatograms were run in a Kodak Chromagram Developing Apparatus 13259 to solvent eluent migrations of 10 to 15 cm. A uV light source was used to detect the solvents.

3.3 Determination of Wavelength Maxima For Solvents

A variable wavelength uV absorption detector was available and used for peak detection in the Varian Model 5000 HPLC system. Therefore, in order to maximize solvent peak responses the wavelengths at which each of the solvents maximally absorbed was determined. Wavelength maxima were obtained for approximately 5 % concentrations of each of the solvent classes in spectral grade n-hexane.

Matched quartz cells were used with one containing the n-hexane reference and the other holding the 5% solvent mixture. The Perkin Elmer 552A uV/Visible spectrophotometer was used to determine this absorbance data.

Solvent classes with accompanying wavelength maxima (the wavelengths at which the HPLC detector was set at for detection) are given in the following table.

SOLVENT CLASS	WAVELENGTH
Aromatics	254 nm
Nitro Compounds	254 nm
Esters	215 nm
Chlorinated Hydrocarbons	215 nm
Ethers	198 nm
Alcohols	198 nm
Ketones	198 nm

3.4 High Performance Liquid Chromatography

The HPLC retention behavior of the solvents was studied using a Varian 5000 High Performance Liquid Chromatograph. This system utilizes a Varian Aerograph variable wavelength uV-100 absorption detector. Chromatograms were recorded on a Hewlett Packard 3393A integrator which labelled peaks with their retention times to an accuracy of .001 minutes. However, data obtained and used in subsequent calculations was taken to an accuracy of .01 minutes due to the inaccuracies involved in the injection method. A FISHERbrand Resolvex column packed with silica particles of 10 μm diameter during the retention studies.

The following gives a summary of the optimum conditions which were used to obtain the solvent retention data.

Operating Conditions

Column:	Resolvex SIL, 4.6 mm i.d. x 25 cm
Instrument:	Varian 5000 HPLC
Mobile Phase:	100% spectral grade n-hexane
Flow Rate:	1.0 mL/min.
Temperature:	Room Temperature
Sample Volume:	20 μL (approximately 5% solvent composition in n-hexane)

Detector wavelength settings were adjusted to respond maximally according to the type of solvent being studied. Detector response and integrator attenuation settings were adjusted according to the sample solvents' molar extinction coefficients.

Data Collection

Bromobenzene and toluene were utilized as test compounds and injected periodically to ensure retention time reliability from day to day. Sample injections were done in triplicate and averages were taken to enhance the reliability of the retention time data.

In order to minimize the number of retention causing interaction possibilities the inert n-hexane was used as mobile phase. Due to the weakness of this solvent as an eluent many polar and moderately polar sample solvents could not be eluted from the column. Therefore, column washings were done periodically to remove the strongly interacting solvents from the silica active sites. These washings were done by flushing the column with up to 20 % isopropanol in n-hexane. After one hour at this composition the column was re-equilibrated for several hours with 100% n-hexane to bring the column back to its original activity level.

3.5 Gas Chromatography

Gas chromatographic analyses were performed in order to study the chromatographic retention behavior of the polar solvents which could not be studied with the weak LC system chosen. A Hewlett Packard 5995 GC/MS was used to accomplish these analyses. This instrument was equipped with an HP-1 capillary column. The column's stationary phase liquid is a crosslinked methyl silicone gum.

The following is a summary of the constant operating conditions which were used to obtain the solvent retention data.

Operating Conditions

Column: 12 m x .2 mm
Coating: HP-1 (Methyl siloxane) .33 um thickness
Column Temperature: 60°C
Injector Temperature: 200°C
Flowrate: Helium, 20 mL/min.
Sample Volume: 1 uL in methanol or dichloromethane
Detection: Mass Spectrum (Total Ion Chromatograph)

Sample injections were done in triplicate and averages of the retention times were taken. The interfaced mass spectrometer was utilized for solvent peak identification and the total ion chroamtograms were used to determine retention time.

3.6 LOTUS 1-2-3 Software

The LOTUS 1-2-3 (Release 2, Lotus Development Corporation copyright 1985) software package was utilized throughout the project in the compilation and manipulation of data. The LOTUS 1-2-3 system disk was used for data table formulation. The LOTUS 1-2-3 Printgraph program was used to create all of the plots which appear in this paper.

3.7 MINITAB Statistical Computing System

The VAX computer's Minitab statistical computing system was used for all of the regression analyses discussed throughout. This system allowed for multiple regression analyses and provided the regression equations along with an analysis of variance (ANOVA).

4.0 RESULTS AND DISCUSSION

Data was collected from several different sources and relied upon in order to obtain a complete list of solvents with the corresponding DN and AN values. The primary source of donor and acceptor numbers is given in the solvent list compiled by Gutmann (9).

Donor numbers for solvents were calculated from sources that provided the following spectroscopic terms and parameters: $\Delta\nu_D$, D(II,I), β, B, and $-\Delta H(BF_3)$. Donor numbers were calculated for each using the following correlation equations:

$$DN = \frac{1.09\ (-\Delta H(BF_3)) - 4.83}{4.184} \qquad [2]$$

$$DN = .20\ (\Delta\nu_D) + 3.03 \qquad [4]$$

$$DN = 10.11\ (D(II,I)) - 12.17 \qquad [5]$$

$$DN = 38.4\ (\beta) - .78 \qquad [6]$$

$$DN = .19\ (B) - .636 \qquad [7]$$

Average donor numbers were determined for each solvent along with an estimate of the error involved in the average DN calculation. The relative error was calculated using the standard deviation, σ, of all of the determined DN values for a solvent. The following

equation provides the sample standard deviation error in the donor number, DN(error):

$$DN\ (error) = \sigma \sqrt{\frac{n}{n-1}} \qquad [21]$$

Table 2 provides a listing of solvents with the corresponding donor numbers both experimentally determined and calculated from the indicated parameters, along with the average DN values and error estimates.

Acceptor numbers for solvents having $E_T(30)$ values were calculated using Schmid's correlation equation [10]. Alcohols and chlorinated hydrocarbons were not considered in the determination of equation [10]. A separate correlation equation was developed by Lan Evans and used to determine AN values for more than 30 alcohol and chlorinated hydrocarbon solvents (25).

Errors in AN values are obtained from Lan Evans' thesis (25). These were calculated from least squares analysis of AN correlation equations. Since two different correlation equations were used, two different estimates of AN error were determined. One equation deals with all solvents except alcohols and chlorinated hydrocarbons and the average AN (error) estimate is $\pm$ 2.86 AN units. The second equation is used only for alcohols and chlorinated hydrocarbons and the AN (error) estimated for these determined AN values is $\pm$ 3.91.

TABLE 2. List of sources from which average Donor Numbers (AVE DN) were calculated.

Compound	exp[a]	$\Delta\nu_0$[b]	D[II,I][c]	B[d]	$-\Delta H_{BF_3}$[e]	Beta[f]	Ave DN	Error[g]
AROMATICS								
n-hexane		3.2					3.2	
benzene		3	3.8	3.5		3.06	3.3	0.38
toluene		3.4	3.5	3.9		3.444	3.6	0.23
HALIDES								
chlorobenzene		2.6		2.2		1.908	2.2	0.35
bromobenzene		2.8		2.2		1.524	2.2	0.64
1,2-dichlorobenzene		0.8					0.8	
chloroform		-0.4	7.4				3.5	5.52
carbon tetrachloride		-1.2	-1.4				-1.3	0.76
dichloromethane		0.6		1.2	1.450		1.1	0.44
1,2-dichloroethane		3.4		2.9			3.2	0.35
1,1-dichloroethane		0.6					0.6	
NITRO COMPOUNDS								
nitromethane	2.7	4.2	10.7	4.8	8.648		6.2	3.33
nitroethane		4.6		5			4.8	0.28
nitrobenzene	4.4	7.2	7.5	3.7	8.169	14.19	7.5	3.73
NITRILES								
acetonitrile	14.1	12.8	14.1	13.2	14.57	11.12	13.3	1.26
propionitrile	16.1	13.4		13.4	14.72		14.4	1.29
acrylonitrile		10.4					10.4	
n-butyronitrile	16.6				14.78		15.7	1.11
benzonitrile	11.9	10.6		12	13.28	14.96	12.6	1.65
phenylacetonitrile	15.1				13.59		14.3	1.07
ESTERS								
methyl acetate	16.5	10.2		10.3	17.80	15.34	14	3.56
ethyl acetate	17.1	10.8		10.9	18.52	16.5	14.8	3.65
methyl chloroacetate		8.4					8.4	
vinyl acetate		7.2					7.2	
methyl acrylate		9					9	
ethyl formate					17.38		17.4	
ethyl benzoate					14.78	14.96	14.9	0.12
4-butyrolactone		16.3					16.3	
KETONES								
acetone	17	15.9		17	18.65	17.65	17.2	1.01
methyl ethyl ketone		14.5		14.3	18.66	17.65	16.3	2.21
diethyl ketone		14.3		12.6	17.67		14.9	2.58
cyclopentanone					19.01	19.18	19.1	0.12
cyclohexanone		16.3		18.7	18.73	19.57	18.3	1.41
acetophenone		14.3		14.1	18.25	18.03	16.2	2.28
di-isopropyl ketone					16.57		16.6	
isopropyl methyl ketone					18.34		18.3	

TABLE 2 (Continued)

Compound	exp	$\Delta\gamma_b$	D[II,I]	B	$-\Delta H_{BF_3}$	Beta	Ave DN	Error
ETHERS								
diethyl ether	19.2	18.7		18.1	19.36	17.26	18.5	0.86
di-n-propyl ether		17.7			19.53	16.88	18	1.36
di-isopropyl ether		18.1			18.80	18.03	18.3	0.43
1,2-dimethoxyethane		17.3					17.3	
anisole		8.2		7.9		7.668	7.9	0.27
phenetole		8				6.9	7.5	0.78
propylene oxide		14.9					14.9	
furan		3.8		4.3			4.1	0.35
tetrahydrofuran	20	21.1	19.56	20.6	22.39	20.34	20.7	1
1,3-dioxalane		14.7					14.7	
1,4-dioxane		18.5	28.5	18	18.14	13.42	19.3	5.54
AMINES								
triethylamine	61	50.7		53.5	34.24	26.48	45.2	14.31
aniline		34.7		33.3			34	0.99
N-methylaniline		33.3					33.3	
N,N-dimethylaniline		32.7			27.28		30	3.83
pyridine	33.1	36.7	32.2	43	32.21		35.4	4.61
2-picoline		39.7			32.95		36.3	4.77
piperidine	51	51.1	28.5	48.7			44.8	10.94
quinoline			30.4				30.4	
2,6-lutidine					24.30		24.3	
AMIDES								
formamide	24		39.9				32	11.24
N,N-dimethylformamid	26.6	24.5	27.7	25.1	27.63	25.71	26.2	1.33
N,N-dimethylacetamid	27.8	25.7		27.4	28.05	28.40	27.5	1.06
N-methyl-2-pyrrolido	27.3				35.19	28.78	30.4	4.19
dimethylethyleneurea					24.61		24.6	
tetramethylurea					27.14	29.17	28.2	1.44
SULFOXIDES								
dimethyl sulphoxide	29.8	31.3	30.1		26.28	28.40	29.2	1.92
tetramethyl sulphone	14.8				12.21		13.5	1.83
di-n-butyl sulphoxide					26.87	31.09	29	2.98
ALCOHOLS								
methanol	19		32.5	12		23.02	21.6	8.56
ethanol	20		30.9	6.5		28.78	21.5	11.09
n-butanol			29.3	24		33.01	28.8	4.53
tert-butanol						38.00	38	
2-propanol						35.7	35.7	
2-phenyl ethanol						22.64	22.6	
ethylene glycol						19.18	19.2	
benzyl alcohol						18.42	18.42	

TABLE 2 (Continued)

Compound	exp	$\Delta\nu_b$	D[II,I]	B	$-\Delta H_{BF_3}$	Beta	Ave DN	Error
CARBONATES								
ethylene carbonate	16.4						16.4	
propylene carbonate					15.56		15.6	
dimethyl carbonate					16.46		16.5	
diethyl carbonate					17.35		17.4	
PHOPHATES								
trimethyl phosphate	23				20.92	27.25	23.7	3.23
triethyl phosphate						28.78	28.8	
tri-n-butyl phosphat	23.7						23.7	
hexamethylphosphoramide				38.1		39.54	38.8	1.02

a Experimental value determined by Gutmann (9).

b DN calculated using Equation [4].

c DN calculated using Equation [5].

d DN calculated using Equation [7].

e DN calculated using Equation [2].

f DN calculated using Equation [6].

g Error is relative error based upon the standard deviations of the individual DN values used in determining the average values.

The error in AN values is much greater than the error in DN values because of the error limitations of the linear regression method that was used to calculate the AN values.

Finally, the AN and DN lists were expanded using the recently obtained data compiled by Beerbower (26). Also included in the list of solvents with AN and DN values are the solvent's δ_d values (Hildebrand's dispersion solubility parameter). The solubility parameter, δ_d, is related to the dispersion interactions which occur in liquids. This data is useful in determining the miscibilty of a solute and solvent. Solvents with similar δ_d values will favorably mix. These values along with donor and acceptor numbers can be used to quantitatively predict the degree of interaction between solvents. The list of accompanying dispersion parameters was also expanded to its completion using data from a paper by Marcus (27). Therefore, the final list of solvents with their corresponding AN and DN values along with the solvents' δ_d values was completed at 106 solvents. See Table 3 for this list. The values which appear in this list are those that are used throughout the project.

The data was first used in the creation of plots of DN vs. AN for all of the solvents comprising the major classes of solvents. These plots illustrate the relative

TABLE 3

LIST OF AN, DN, AND Sd

SOLVENT[a]	AN[b]	DN[c]	S_d[d]
HYDROCARBONS			
1. n-hexane	0[x]	3.2	7.3
2. c-hexane	0	0	7.3
3. benzene	8.2[x]	3.3	9
4. toluene	3.2	3.6	8.8
5. 1,2-dimethylbenzene	3.7	3.8	8.7
6. 1,3-dimethylbenzene	2.4	3	8.7▲
7. 1,3,5-trimethylbenzene	2.2	10[+]	8.8
HALIDES			
8. 1,2-dichloroethane	16.7[x]	3.2	9.3
9. 1,1-dichloroethane	10.3	0.6	8.1
10. dichloromethane	22.4	1.1	8.9
11. carbontetrachloride	9.6	1.3	8.7
12. chloroform	19.4	3.5	8.7
13. bromobenzene	7.9	2.2	10
14. chlorobenzene	7.9	2.2	9.3
15. fluorobenzene	8.6	3[+]	(8.6)
16. iodobenzene	8.4	4[+]	(9.1)
17. 1,2-dichlorobenzene	8.6	0.8	9.4
NITRO COMPOUNDS			
18. nitromethane	20.5	6.2	7.7
19. nitroethane	15.7	4.8	7.8
20. nitrobenzene	14.8[x]	7.5	9.8
NITRILES			
21. acetonitrile	18.9[x]	13.3	7.5
22. propionitrile	15.9	14.4	7.5
23. acrylonitrile	19.7	10.4	8
24. n-butyronitrile	15.1	15.7	7.5
25. benzonitrile	15.5[x]	12.6	8.5
26. phenylacetonitrile	14.8	14.3	9.2▲
ESTERS*			
27. methylacetate	10.7[x]	14	7.6
28. ethylacetate	9.3[x]	14.8	7.7
29. vinylacetate	8.5	7.2	(7.5)
30. propylacetate	7.9	16[+]	(7.5)
31. ethylbutryate	9.1	16.8	(7.5)
32. methylacrylate	16.9	9	(7.7)
33. ethylformate	12.2	17.4	7.6
34. ethylbenzoate	8.6	14.9	8.9 ▲

TABLE 3 (continued)

35. methylchloroacetate	13.7	8.4	(8.5)
36. 4-butyrolactone	16.6	16.3	9.3
KETONES			
37. 2-propanone	12.5[X]	17.2	7.6
38. 2-butanone	12.8	16.3	7.8
39. 3-pentanone	10.2	14.9	7.7
40. diisopropylketone	9.4	16.6	(7.4)
41. 3-methyl-2-butanone	12.2	18.3	(7.4)
42. cyclopentanone	10.3	19.1	(8.6)
43. cyclohexanone	10.8	18.3	8.7
44. acetophenone	12.8	16.2	9.6
ETHERS			
45. diethyl ether	3.9[X]	18.5	7.1
46. diisopropyl ether	3.3	18.3	6.7[▲]
47. dipropyl ether	3.3	18[+]	(7.2)
48. di-n-butyl ether	2.6	18.1	7.4
49. dimethoxyethane*	10.2[X]	17.3	7.7
50. phenylmethyl ether	7.5	7.9	8.7
51. propylene oxide	10.8	14.9	(7.4)
52. furan	3.3[X]	4.1	8.7
53. tetrahydrofuran	8[X]	20.7	8.2
54. 1,4 dioxalane*	8.4	19.3	9.3
55. 1,3 dioxalane*	15.1	14.7	(8.4)
56. phenylethyl ether	6.4	7.5	(8.6)
AMINES			
57. t-butylamine	7	57.5[+]	(7.5)
58. diethylamine	9.4[X]	50[+]	7.3[▲]
59. triethylamine	1.4[X]	45.2	(7.3)
60. ethylenediamine*	20.9[X]	55[+]	(8)
61. aniline	16.6	34	9.5
62. N-methylaniline	14.3	33.3	9.3[▲]
63. N,N-dimethylaniline	8.5	30	8.9[▲]
64. 2-chloroaniline	18.2	31[+]	(9.3)
65. pyridine	14.2[X]	35.4	9.3
66. 2-picoline	8.9	36.3	(9.7)
67. 2,6-lutidine	6.8	24.3	(10.1)
68. piperidine	5	44.8	8.6[▲]
69. quinoline	10.3	30.4	9.5
AMIDES*			
70. formamide	39.8[X]	32	8.4
71. N-methylformamide	32.1[X]	49[+]	8.4[▲]
72. N,N-dimethylformamide	16[X]	26.2	8.5
73. N,N-dimethylacetamide	13.6[X]	27.5	8.2
74. N-methyl-2-pyrrolidone	13.3[X]	30.4	8.8
75. 1-formylpiperidine	5.3	28.6	(8.8)
76. dimethylethylurea	14.3	24.6	
77. tetramethylurea	12.4	28.2	8.2
SULFIDES			
78. carbondisulfide	1.5	3.8	10

TABLE 3 (continued)

SULFOXIDES			
79. dimethyl sulfoxide	19.3[X]	29.2	9
80. tetramethylene sulfone*	19.2[X]	13.5	
81. dibutyl sulfoxide	9	29	(7.3)
CARBONATES*			
82. ethylene carbonate	22.2	16.4	9.5
83. propylene carbonate	18.3[X]	15.6	9.8
84. dimethyl carbonate	12.5	16.5	(8.5)
85. diethyl carbonate	6.2	17.4	8.1
PHOSPHATES*			
86. trimethyl phosphate	16.3[X]	23.7	8.2
87. triethyl phosphate	13.3	28.8	8.2
88. tri-n-butyl phosphate	9.9[X]	23.7	8
89. hexamethyl phosphoramid	11.4	38.8	9
ALCOHOLS			
90. methanol	41.3[X]	21.6	7.4
91. ethanol	37.1[X]	21.5	7.7
92. 2-propanol	35.5[X]	35.7	7.7
93. 1-butanol	36.8[X]	28.8	7.8
94. 2-methyl-2-propanol	27.1[X]	38	(7.3)
95. 1-pentanol	34.3	26.2	7.8
96. 3-methyl-1-butanol	34.1	32	(7.6)
97. 2-methyl-1-butanol	31.1	32	(7.5)
98. 1-octanol	33.1	32	7.7
99. cyclohexanol	30.1	25	8.5
100. benzyl alcohol	36.8	18.4	9
101. 2-phenyl ethanol	34.9	22.6	(8.9)
102. ethylene glycol*	44.9	19.2	8.3
103. glycerin	46	19[+]	8.5
104. water	54.8[X]	33	7.6
MISCELLANEOUS			
105. benzaldehyde	28	16[+]	(9.1)
106. acetic anhydride	16.1	10.5	7.8[▲]

a * indicate a multiple interaction sites.

b AN values are calculated from Table 4, those with X indiccate experimental AN values.

c DN values are averages from Table 2, those with + from Marcus (30)

d S_d values from Barton(15), those values with parenthesis were approximated using vau Krevelen's additivity values(18), those values with ▲ are form Beerbower(3)

electron pair donor and acceptor strengths for each of the individual solvents within each group. Figures 9 - 18 are the plots for these various classes. Note that the numbered data points correspond to the numbers assigned to each of the solvents in Table 3. Figure 19 represents all of these plots with regions shown for each of the classes of solvents in Table 3. This arrangement is termed a sorting map and serves to indicate the donor and acceptor strengths of each of the classes relative to the others. For example, hydrocarbons have very low donor and acceptor ability and are located near zero on both axes. Amines, which are highly donating, are found high on the DN scale and generally low on the AN scale.

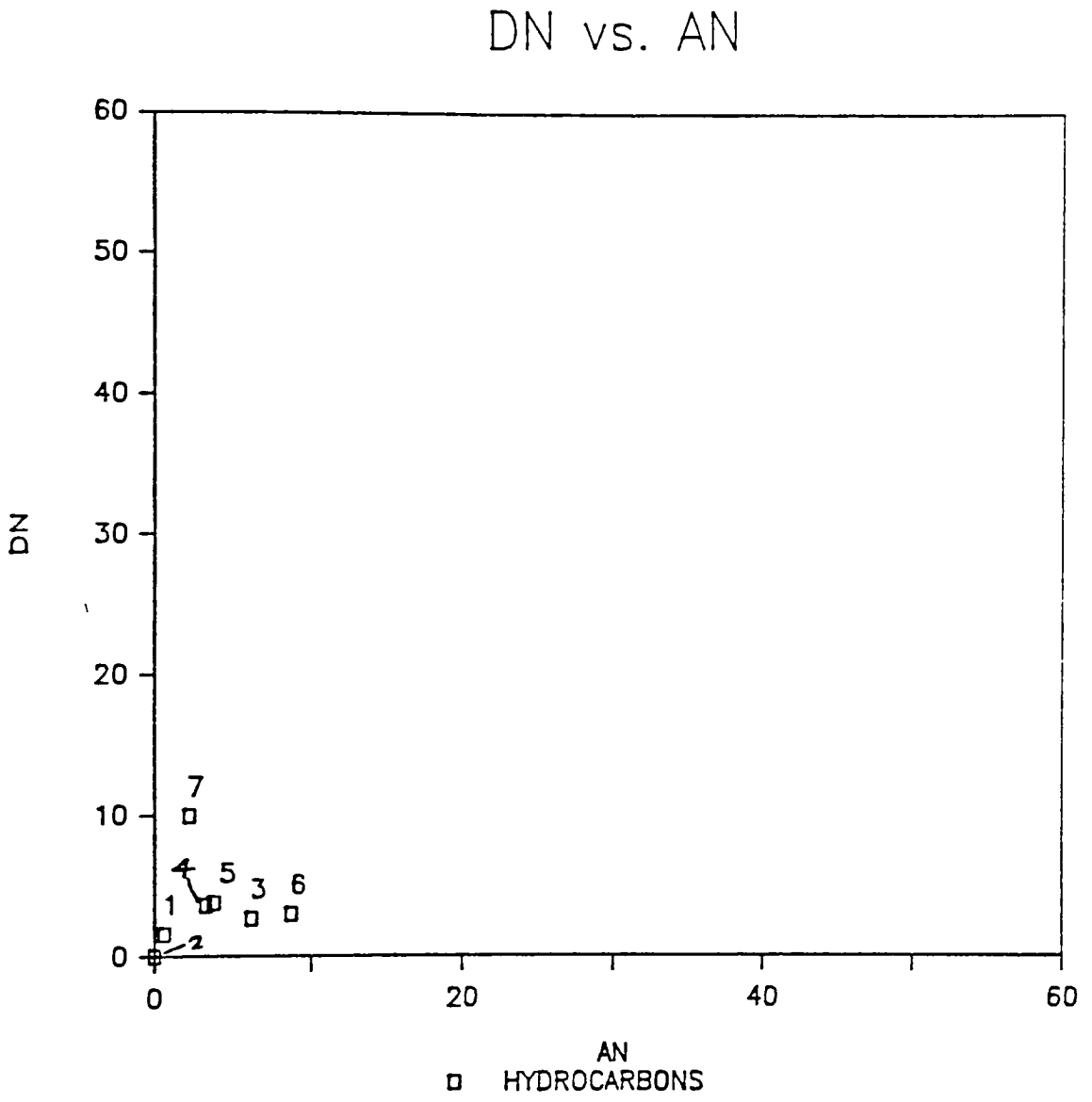

Figure 9. Plot of the donor number (DN) vs. the acceptor number (AN) for hydrocarbon solvents (1-7).

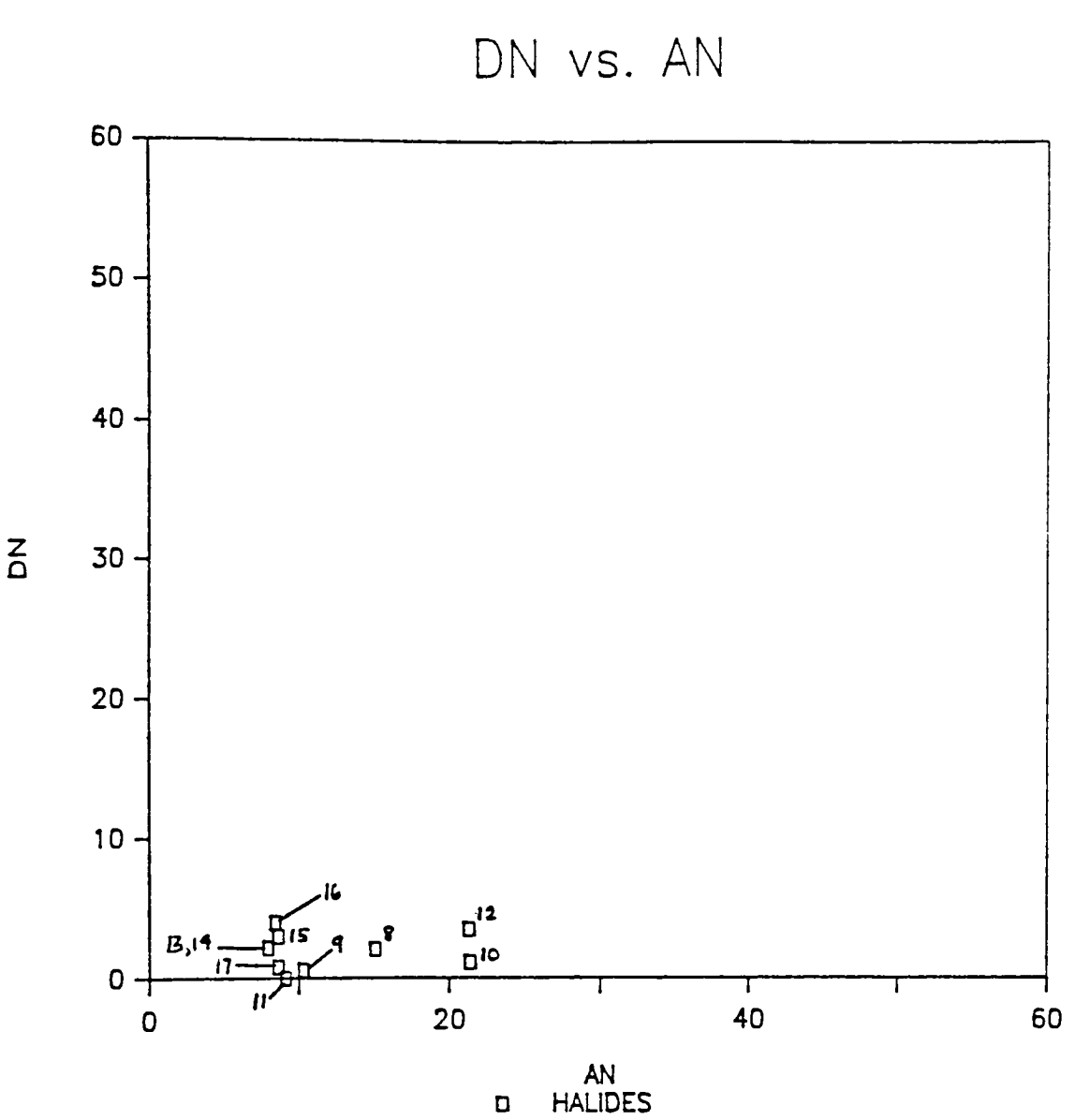

Figure 10. Plot of the donor number (DN) vs. the acceptor number (AN) for halide solvents (8-17).

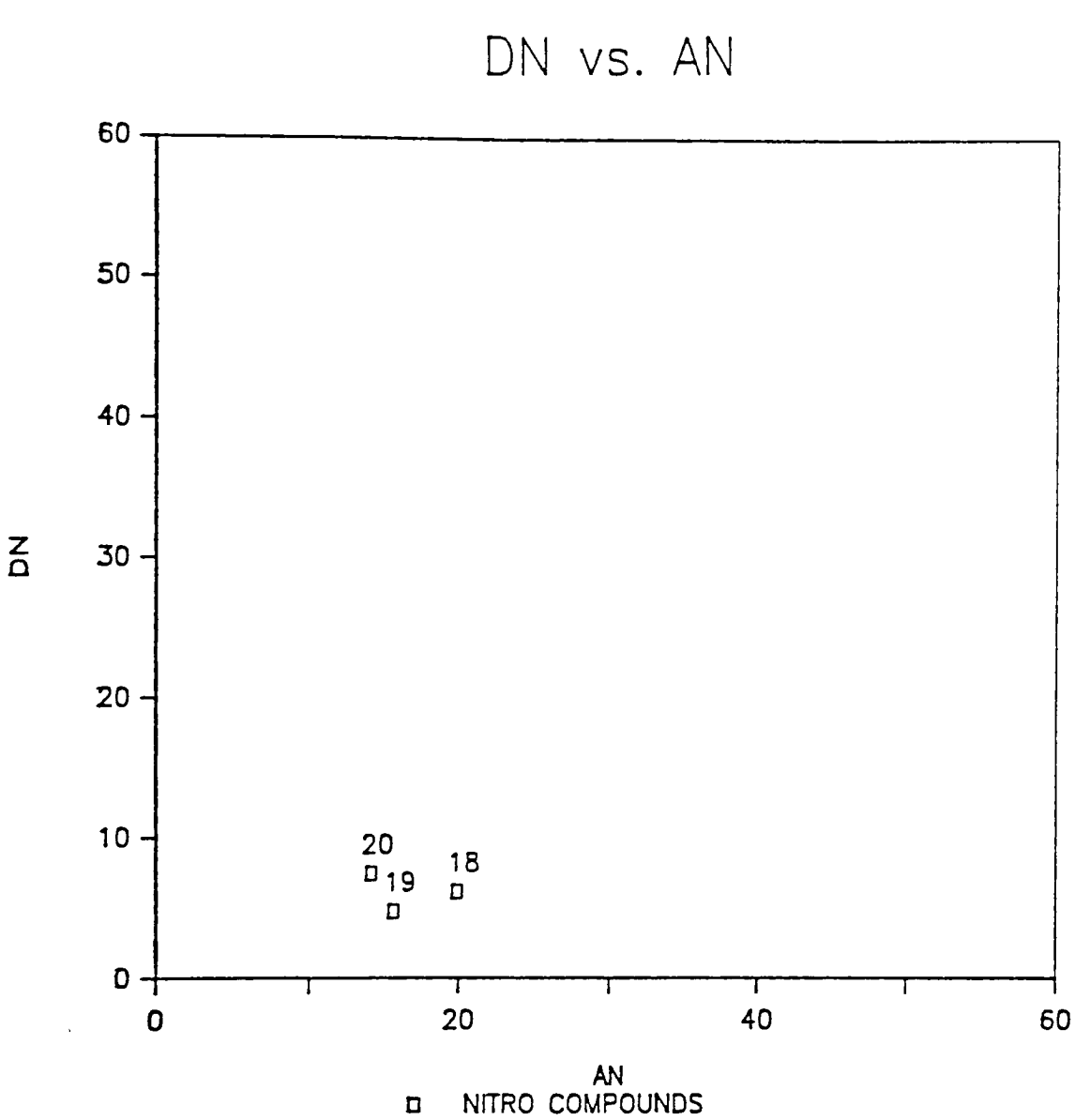

Figure 11. Plot of the donor number (DN) vs. the acceptor number (AN) for nitro group containing solvents (18-20).

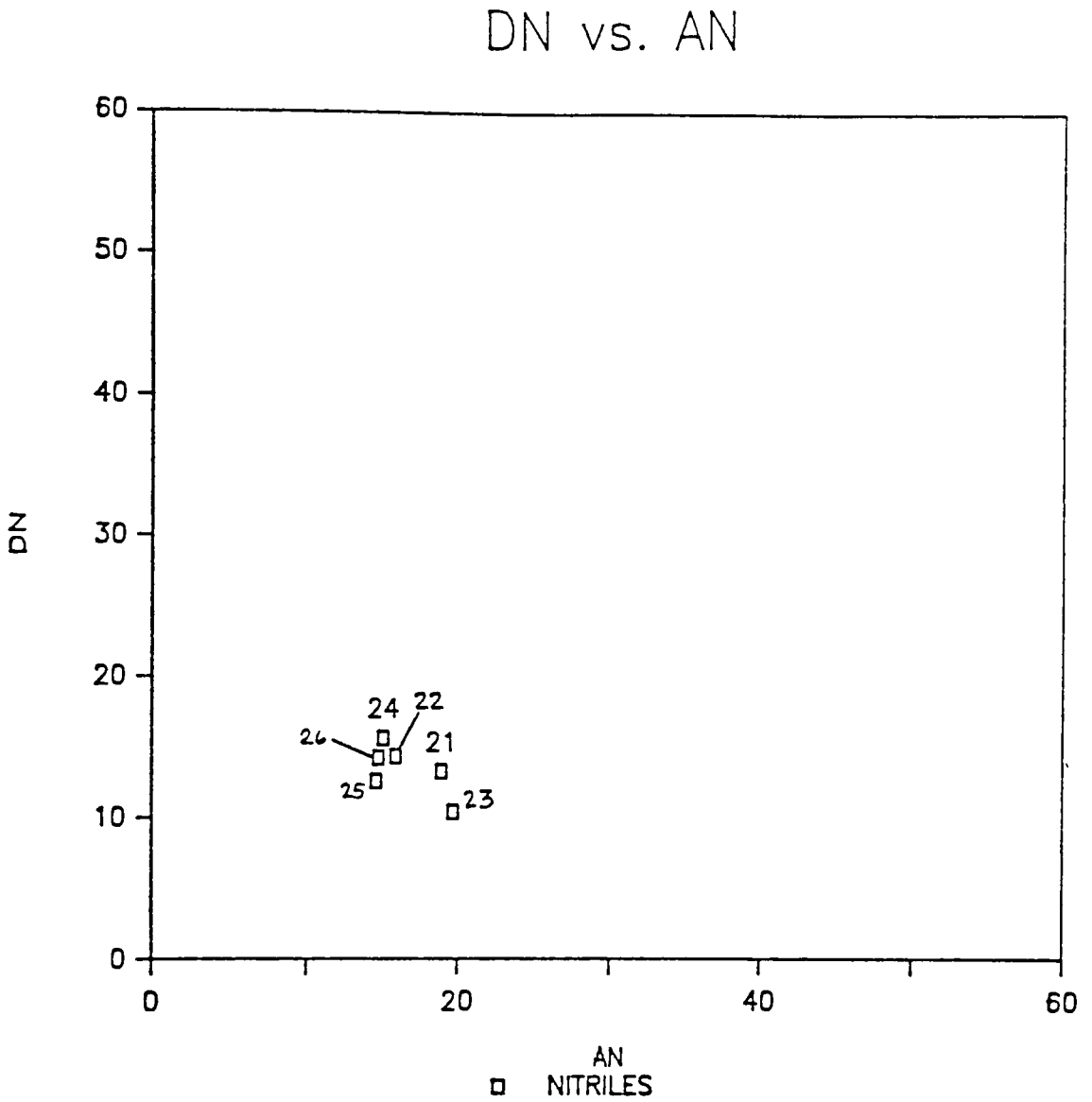

Figure 12. Plot of the donor number (DN) vs. the acceptor number (AN) for nitrile solvents (21-26).

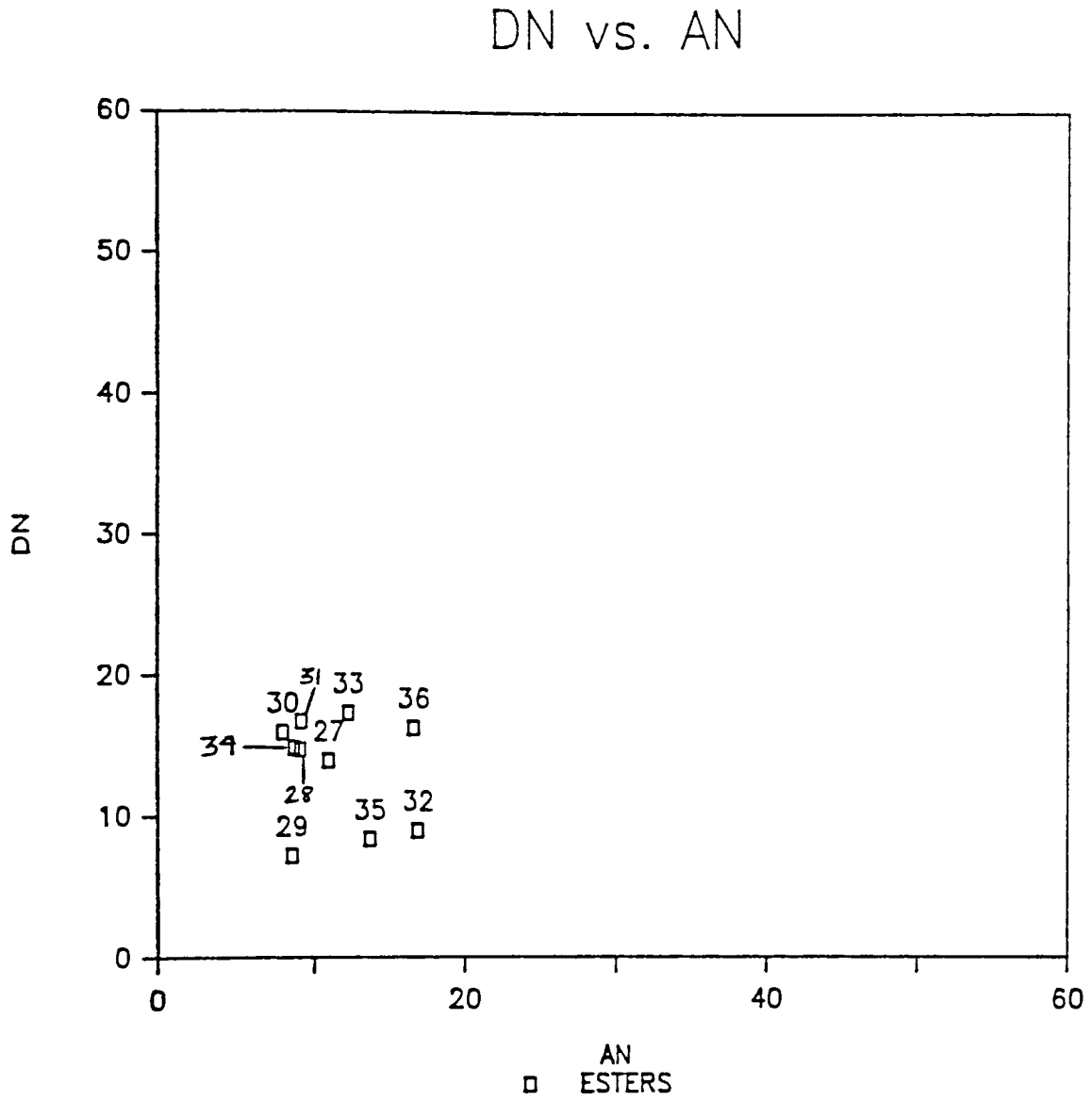

Figure 13. Plot of the donor number (DN) vs. the acceptor number (AN) for ester solvents (27-36).

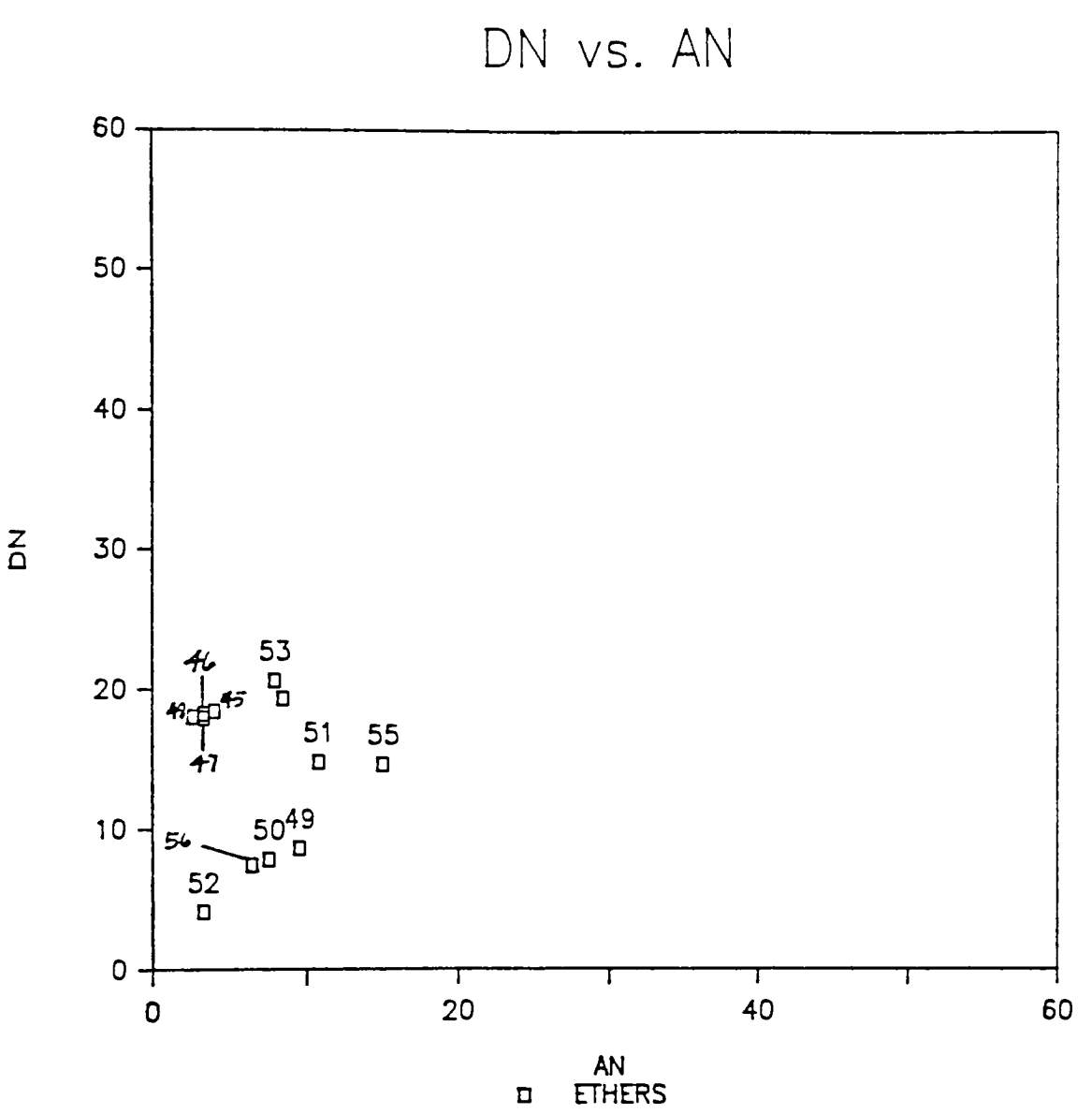

Figure 14. Plot of the donor number (DN) vs. the acceptor number (AN) for ether solvents (45-56).

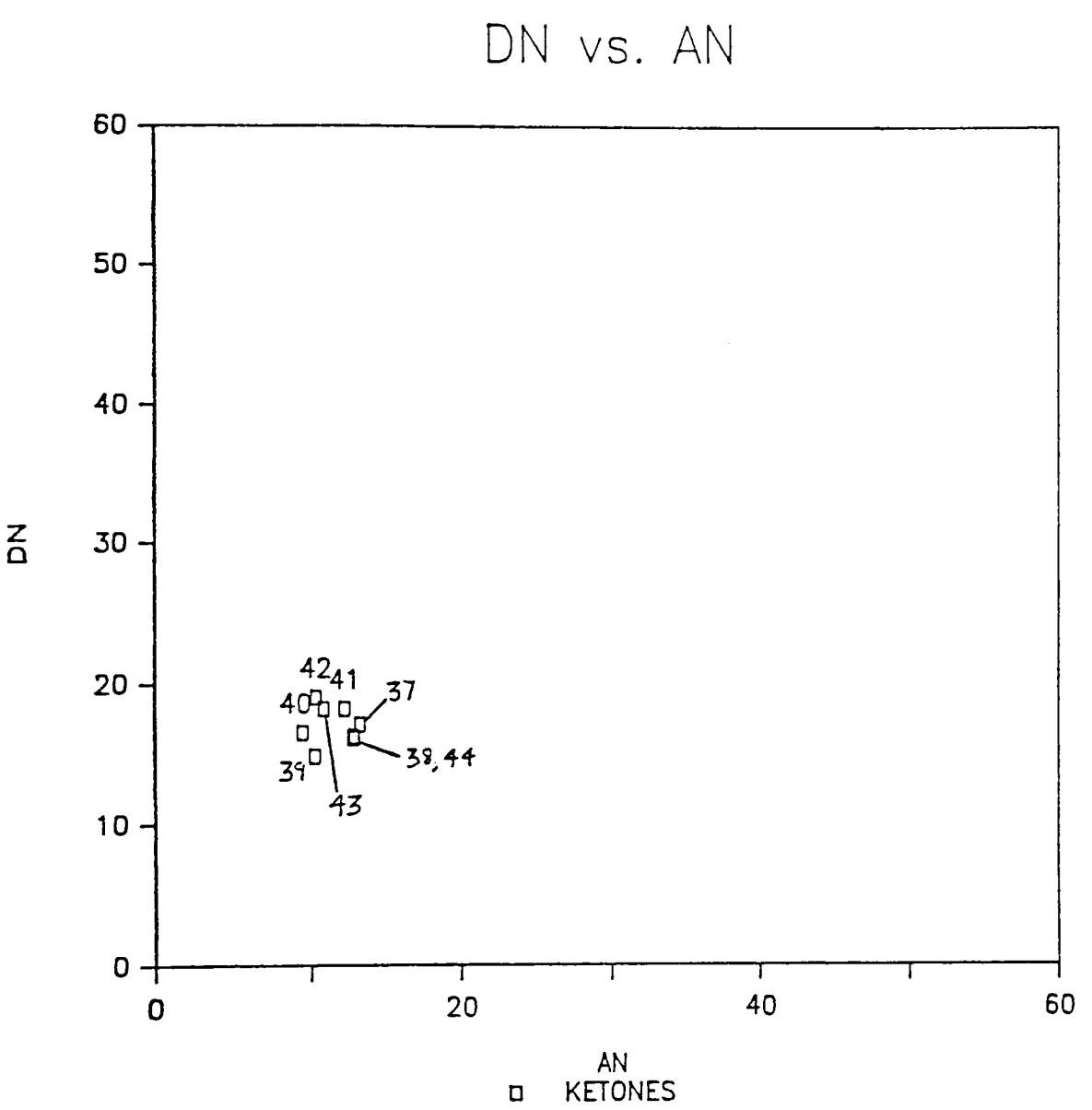

Figure 15. Plot of the donor number (DN) vs. the acceptor number (AN) for ketone solvents (37-44).

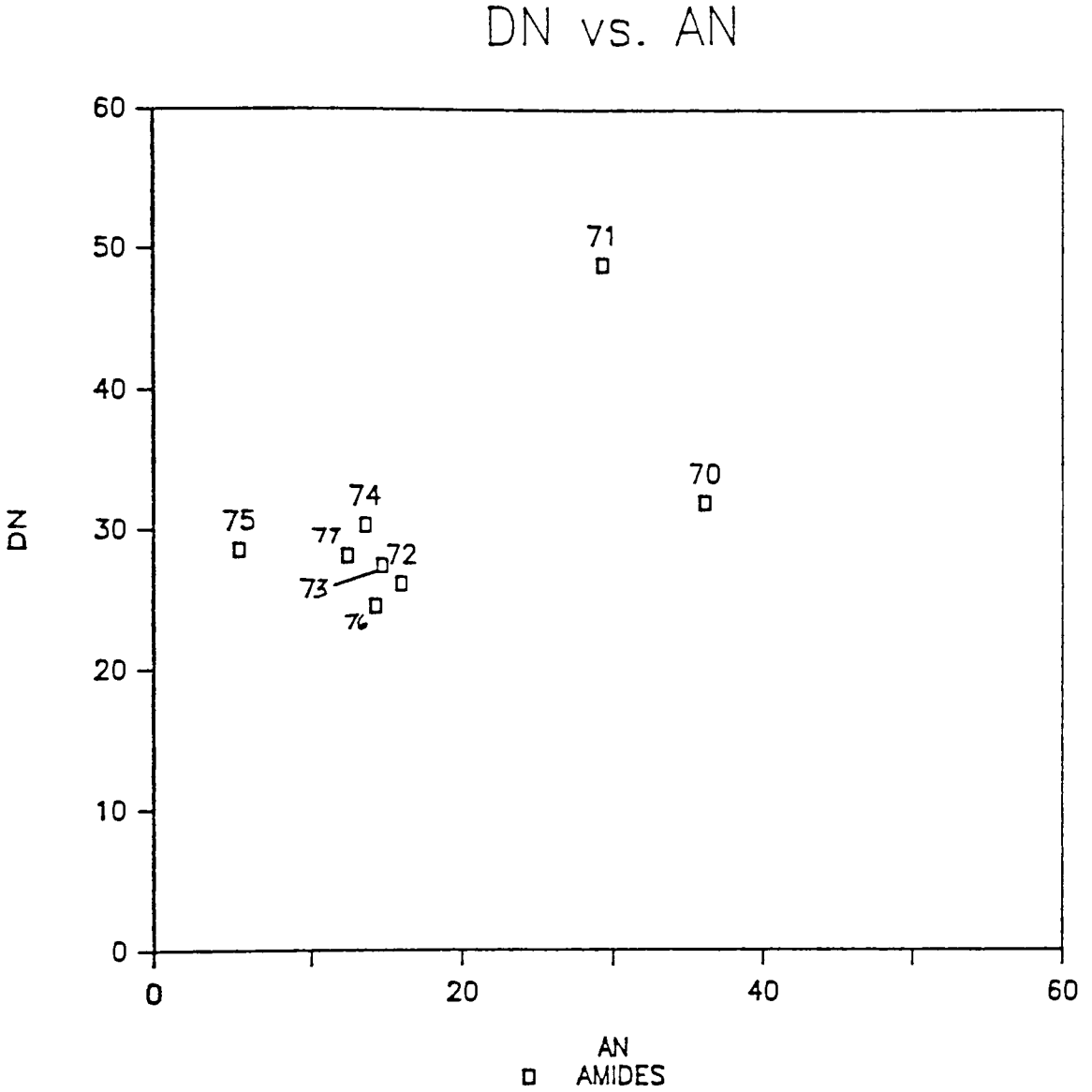

Figure 16. Plot of the donor number (DN) vs. the acceptor number (AN) for amide solvents (70-77).

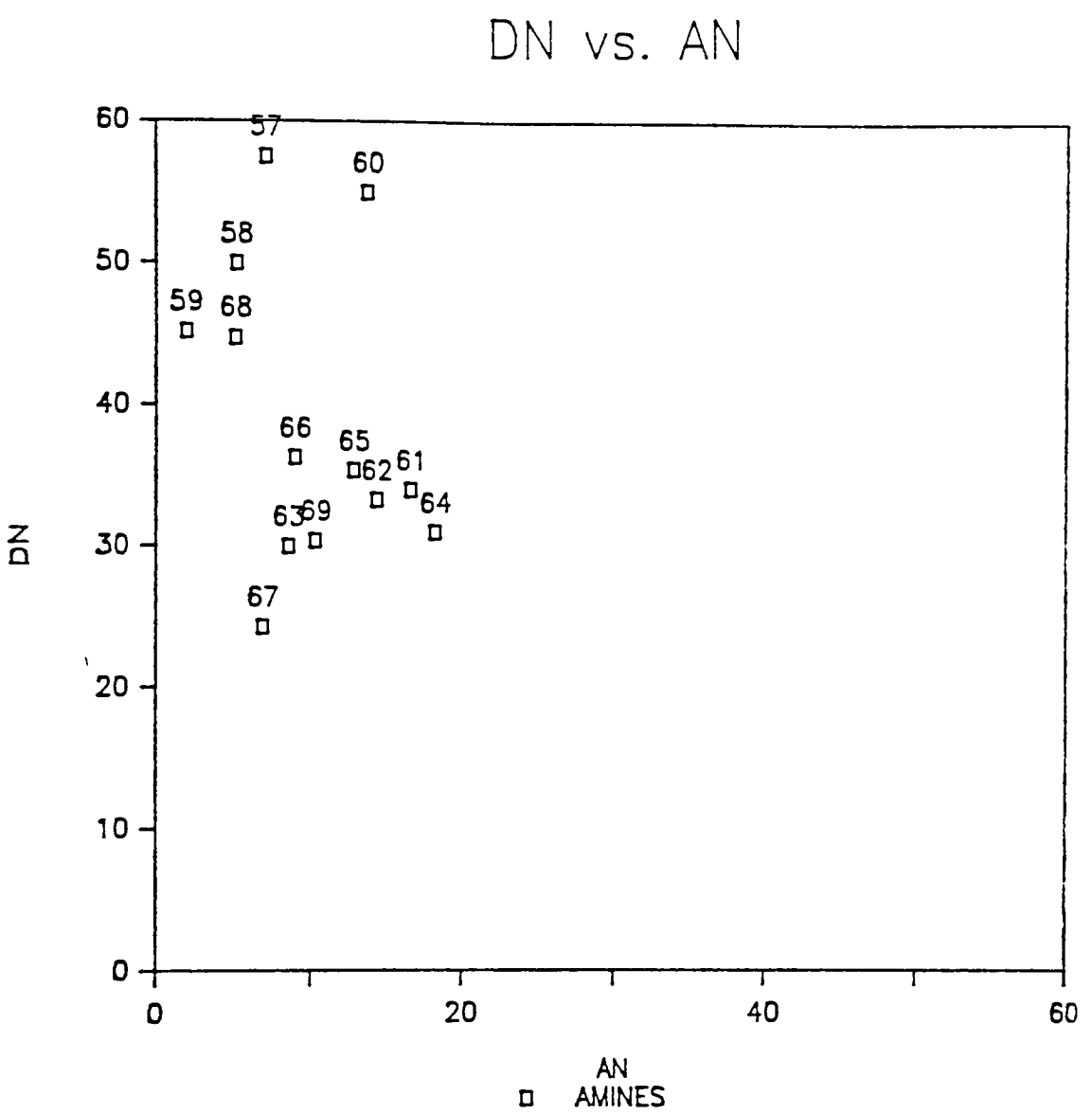

Figure 17. Plot of the donor number (DN) vs. the acceptor number (AN) for amine solvents (57-69).

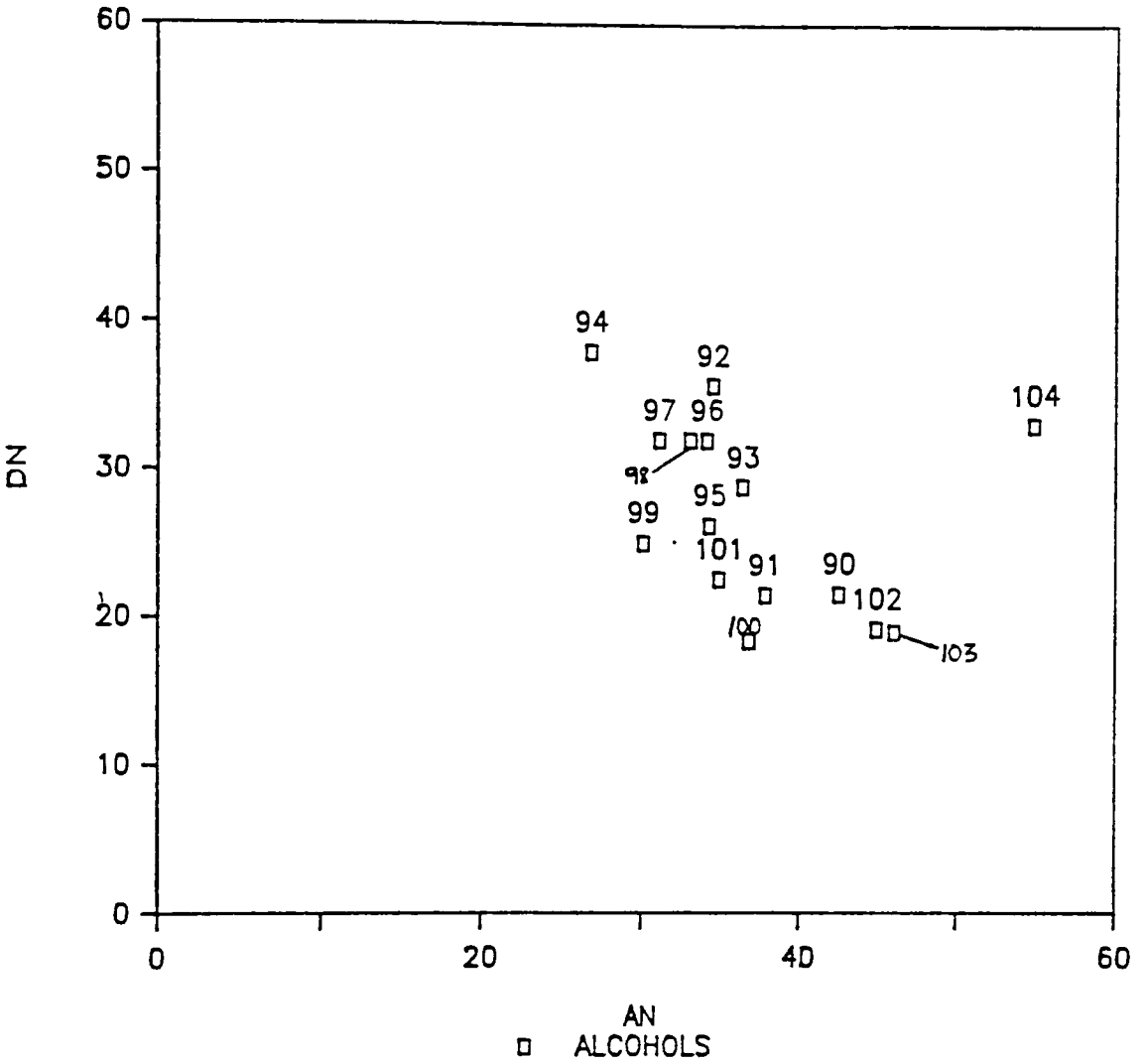

Figure 18. Plot of the donor number (DN) vs. the acceptor number (AN) for alcohol solvents (91-104).

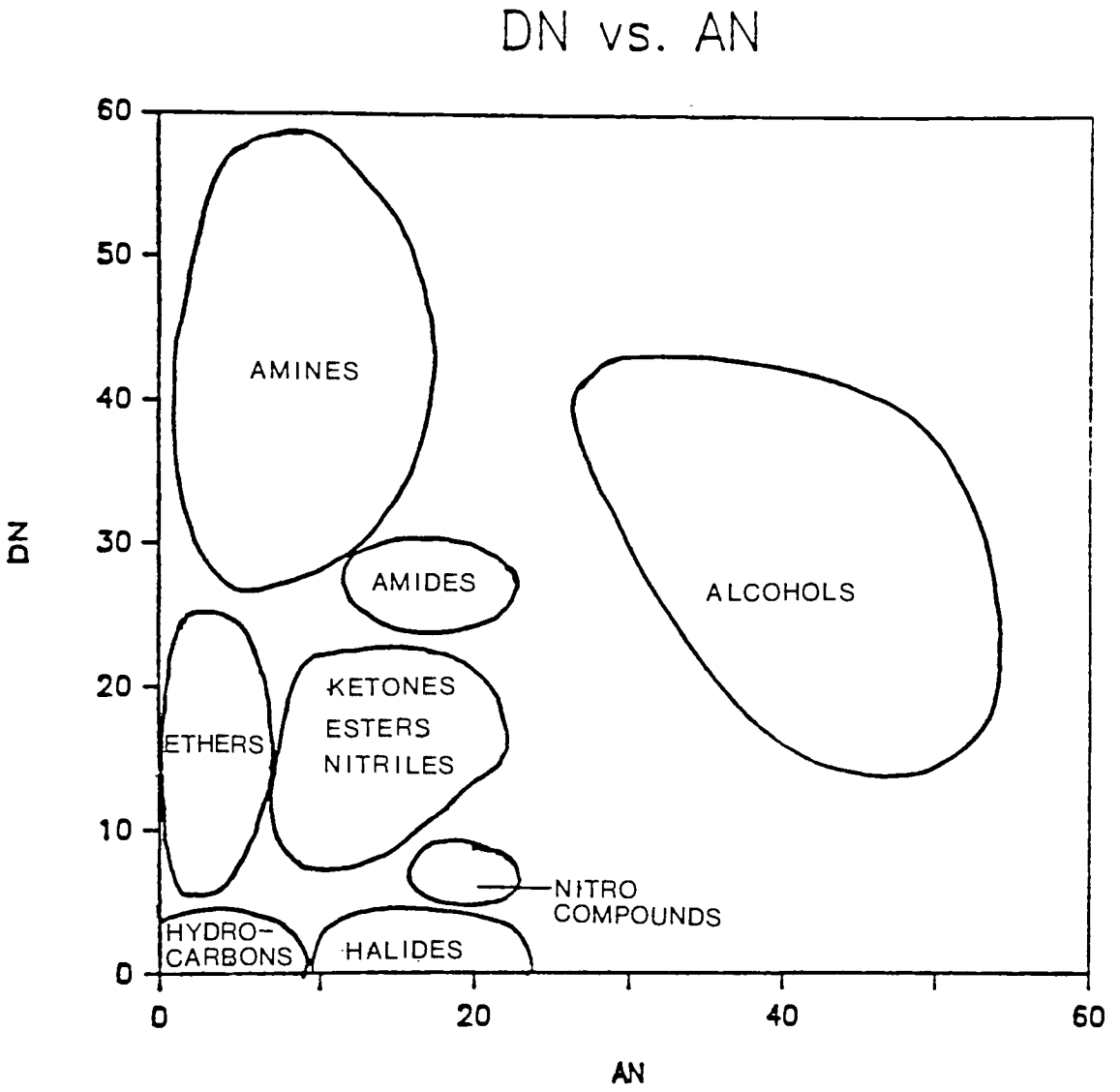

Figure 19. Sorting map plot of the donor number (DN) vs. the acceptor number (AN) for the indicated solvent classes.

4.1 LIQUID CHROMATOGRAPHIC STUDIES

The chosen liquid chromatographic system (silica stationary phase with hexane mobile phase) was scouted through a thin layer chromatographic study. R_f values were collected for a number of aromatic solvents. Table 4 shows a list of these solvents with accompanying R_f values.

TABLE 4. TLC Retention Data

Solvent	R_f
1,2-dichlorobenzene	.98
nitrobenzene	.29
benzonitrile	.27
ethyl benzoate	.27
acetophenone	.33
aniline	.18
benzyl alcohol	.15
benzaldehyde	.09

The solvents listed in Table 4 were chosen because of their higher boiling points and thus not evaporate upon the running of the thin layer chromatogram.

Equation [22] was used in order to determine the correlation between thin layer chromatographhic retention and the AN and DN values.

$$(1-R_f) = AN\ (a) + DN\ (b) \qquad [22]$$

The $(1-R_f)$ relation is used to compensate for the inverse relationship that exists between R_f and t_r . Equation [22] is in the form of the proposed correlation for retention given by equation [23].

$$t_r = AN\ (a) + DN\ (b) \qquad [23]$$

The (a) and (b) in these equations are constants which are derived from linear regression analysis of the data. The (a) and (b) terms quantitatively describe the relative contributions of electron accepting and electron donating interactions between the solvent and the stationary phase in the chromatographic retention process.

4.1.1 SIMPLE LINEAR REGRESSION ANALYSIS

The first method by which the data was analyzed was through rearrangement of equation [22] to obtain an equation of the simple linear relationship, y = mx + b:

$$(1-R_f)/AN = (DN/AN)\ (b) + (a) \qquad [24]$$

where $(1-R_f)/AN$ is the y term, (DN/AN) is the x term, (b) the slope, and (a) the y-intercept of the resulting plot.

Using the TLC data for the solvents given in Table 4 a plot of $(1-R_f)/AN$ vs. (DN/AN) was carried out and is shown in Figure 20. Simple linear regression analysis resulted in a correlation coefficient (R^2) of 0.57. This poor linearity result reflects the crudeness of the method and the inaccuracies involved in the calculation of R^2 values. Through visual inspection of the data points on the plot one can see that aniline (solvent #61) deviates from the linearity that exists amongst the other data points. Exclusion of this data point results in improved linearity (R^2= 0.7). The highly electron-donating aniline interacts so strongly with the silica such that migration on the silica is very limited.

This TLC study demonstrated that only relatively nonpolar solvents could be analyzed using the chosen LC system. Even moderately polar solvents would bind strongly to active silica sites. Since hydrogen bonding occurs at the silica hydroxyl sites solvents with large

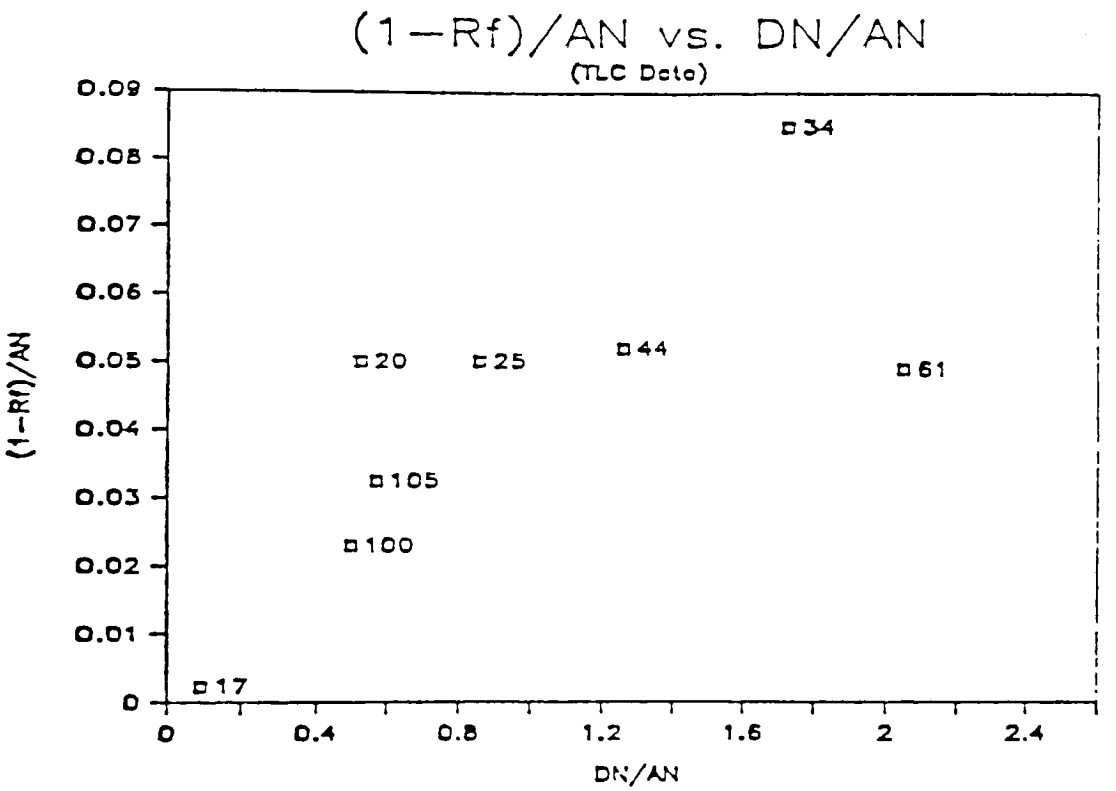

Figure 20. Plot of (1 - Rf)/AN vs. DN/AN using TLC retention data for various aromatic solvents.

LINEAR REGRESSION ANALYSIS

REGRESSION EQUATION:

$$\frac{(1-Rf)}{AN} = (.0272)\frac{DN}{AN} + .0172$$

SLOPE = b = .0272
Y-INTERCEPT = a = .0172
R-SQUARE FACTOR (% LINEARITY) = 57%

donor numbers (DN > 20) are not readily eluted by the weak hexane mobile phase.

The contributions of the AN and DN parameters to the solvent's retention is given by the calculated terms (a) and (b), respectively. In the TLC study the value of (b) is almost twice as great as (a) which indicates that the donor interactions are more important than the acceptor interactions. Since this TLC study showed promising results the system of silica stationary phase and hexane mobile phase was used to continue the project using HPLC retention data.

HPLC retention times were collected for a series of solvents possessing low donor and acceptor numbers. The experimentally determined retention data is given in Table 5.

Table 5. HPLC Retention Data

Solvent	t_r (min)	(±) Error (min)
Benzene	3.73	.04
Toluene	3.71	.04
o-xylene	3.80	.04
m-xylene	3.40	.02
1,2-dichloroethane	4.03	.02
dichloromethane	4.44	.04
carbon tetrachloride	3.30	.02
chloroform	4.06	.02
bromobenzene	3.97	.02
fluorobenzene	4.03	.02
iodobenzene	3.98	.02
nitrobenzene	14.42	.10
benzonitrile	14.83	.50
acetophenone	16.13	.60

The error listed is absolute error and is based upon the deviations from the 3 retention times obtained for each

injection.

Equation [23] was applied and rearranged to give equation [25].

$$(t_r/AN) = (DN/AN)\ (b) + (a) \qquad [25]$$

A plot of (t_r/AN) vs. (DN/AN) results in a slope equal to (b) and a y-intercept equal to (a). Where (a) and (b) again, simply represent the constants used to correlate AN (factor (a)) and DN (factor (b)) to retention times. Figure 21 represents this plot with the linear regression analysis given. This linear regression analysis gave a correlation coefficient of .901, slope = .833, and y-intercept = .211. This percent linearity of greater than 90% indicates a linear realtionship between HPLC retention time, DN, and AN. Thus, the AN multiplication factor (a) is equal to the y-intercept, .211, and the DN multiplication factor (b) is equal to the slope, .833. Again, this shows that the solvent's donor interaction capability is the primary contributor to a solvent's retention on silica in a normal phase system employing a very nonpolar mobile phase such as hexane.

In order to show reproducibility of the retention data and the correlation equation another set of data was collected for a similar group of solvents . Again, good linearity was obtained (R^2 = .91). (a) equalled .720 and (b) was .103.

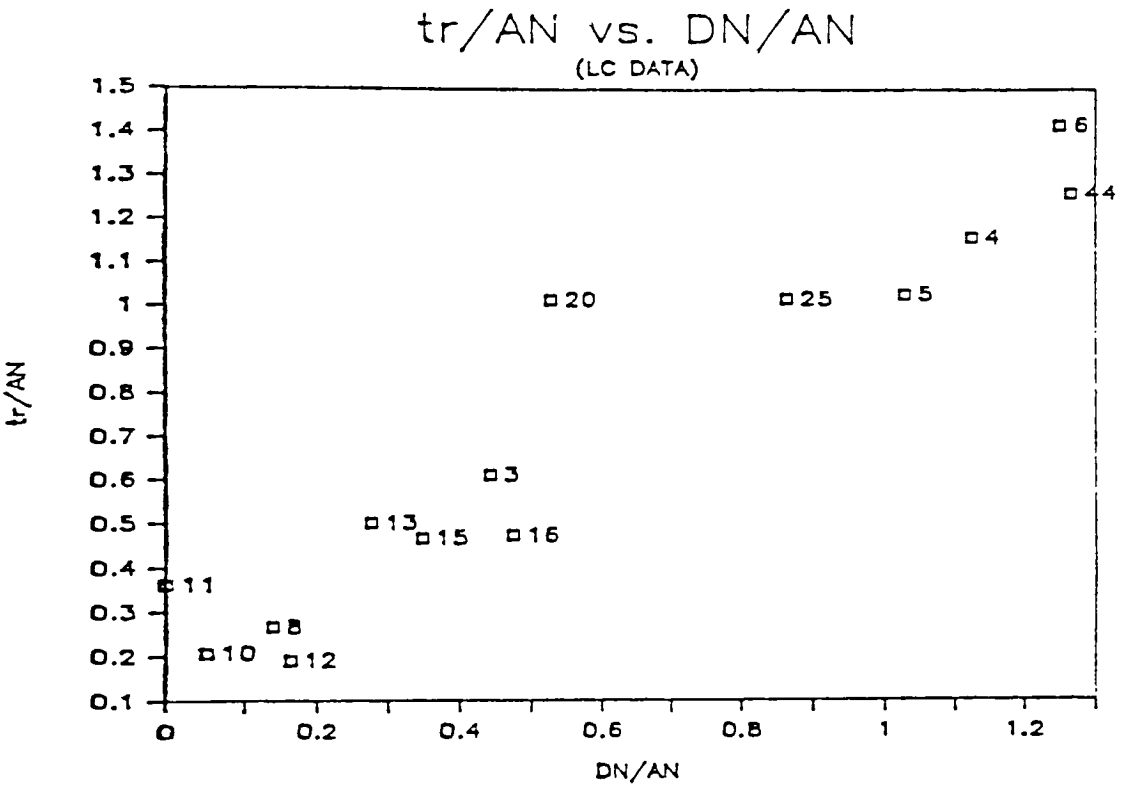

Figure 21. Plot tr/AN vs. DN/AN using HPLC retention data for hydrocarbons, halides, and substituted aromatics.

LINEAR REGRESSION ANALYSIS

REGRESSION EQUATION:

$$\frac{tr}{AN} = (.833)\frac{DN}{AN} + .211$$

SLOPE = b = .833
Y-INTERCEPT = a = .211
R-SQUARE FACTOR (% LINEARITY) = 90%

4.1.2 MULTIPLE REGRESSION ANALYSIS

In order to improve the linearity of the relationship another form of equation [23] was devised. This new adjustment includes an intercept term, c, and is given by equation [26].

$$t_r = AN\ (a) + DN\ (b) + (c) \qquad [26]$$

A computerized regression analysis is done such that equation rearrangement and subsequent plotting is not necessary. The multiple regression analysis was provided by the MINITAB statistical system for the retention data from Table 5. Equation [27] gives this determined equation.

$$t_r = .95\ (DN) + .13\ (AN) + .42 \qquad [27]$$

The resulting correlation coefficient was 0.87, meaning that the inclusion of an intercept term did not significantly improve the correlation of the data.

In dealing with chromatographic retention times in this type of study there generally exists a log relationship. Therefore, in a further attempt to improve correlation the $\log_{10}$ was taken of each of the solvent's retention times. A similar regression analysis was performed resulting in equation [28]. However, poorer correlation was obtained with R^2 of .835.

$$\log t_r = .058\ (DN) + .088\ (AN) + .361 \qquad [28]$$

Due to the fact that the solvents used in this HPLC study are comprised mainly of nonpolar substituents a parameter which accounts for this was included. As discussed in the introduction section , the π^* parameter is best suited to describing the solvent polarizabilty interactions. This is an especially important contribution for the aromatics due to the polarizable π-electron system of the aromatic ring. Inclusion of the term into the equation results in an equation of the form of equation [29].

$$t_r = AN\ (a) + DN\ (b) + \pi^*(c) + INT \qquad [29]$$

Multiple regression analysis of the retention data for the solvents listed in Table 5 resulted in equation [30].

$$t_r = .268(AN) + .89(DN) - 3.22(\pi^*) + .56 \qquad [30]$$

This adjustment in the equation greatly enhanced the correlation, with R^2 equal to .982.

Table 6 provides a listing of the π^* values for the solvents of the HPLC study data set along with the experimental and predicted retention times. Also listed in Table 6 is the error estimate associated with retention time predictions. This value is based on the errors inherent in the evaluation of the AN and DN

Table 6. Parameters (π^*, DN, and AN) Used With Equation [30] To Predict LC Retention Times, t_r(calc)

SOLVENT	π^*	DN	AN	t_r(exp) (min)	t_r(calc) (min)	t_r(error) (min)
Benzene	0.19	2.7	6.1	3.73	3.78	1.52
Toluene	0.14	3.6	3.2	3.71	3.97	1.51
Bromobenzene	0.39	2.2	7.9	3.97	3.18	1.61
m-Xylene	0.07	3.0	2.4	3.4	3.44	1.53
Dichloromethane	0.62	1.1	21.4	4.44	5.07	1.54
Fluorobenzene	0.22	3.0	8.6	4.03	4.62	1.55
Acetophenone	0.50	16.2	12.8	16.13	16.59	2.61
Benzonitrile	0.50	12.6	14.6	14.83	13.87	2.15
Carbon Tetrachloride	0.08	0.0	9.1	3.3	2.54	2.15
1,2-Dichloroethane	0.81	2.1	15.1	4.03	3.66	2.05
Iodobenzene	0.41	4.0	8.4	3.98	4.85	1.55

parameters. The calculated retention times, denoted by t_r(calc), are determined by insertion of the appropriate solvent data into equation [27]. A plot of t_r(exp) vs. t_r(cal) is given in Figure 22. This plot illustrates the linear relationship between the actual retention times for a solvent and the retention time predicted based on the solvent's π^*, DN, and AN values.

The best correlation of this data is obtained by including the $\log_{10} t_r$ in the relationship. The log relationship applied to equation [30] improves the correlation. Equation [31] represents this correlation.

$$\log t_r = .013(AN) + .043(DN) - .089(\pi^*) + .394 \qquad [31]$$

This equation gives a 98.9 % linear relationship. A plot of log t_r(exp) vs. log t_r(calc) is given in Figure 23.

π^* values are orders of magnitude lower than AN and DN values and to get an understanding of the relative contributions of π^*, DN, and AN to retention in these equations relative evaluations of (a), (b), and (c) are calculated. These partial regression coefficients are denoted by a', b', and c'. As an example a' is calculated using the following equation:

$$a' = |a| \left(\frac{\sum_{i=1}^{n} (AN_i - \overline{AN})^2}{\sum_{i=1}^{n} (\log t_{r_i} - \overline{\log t_r})^2} \right)^{1/2} \qquad [32]$$

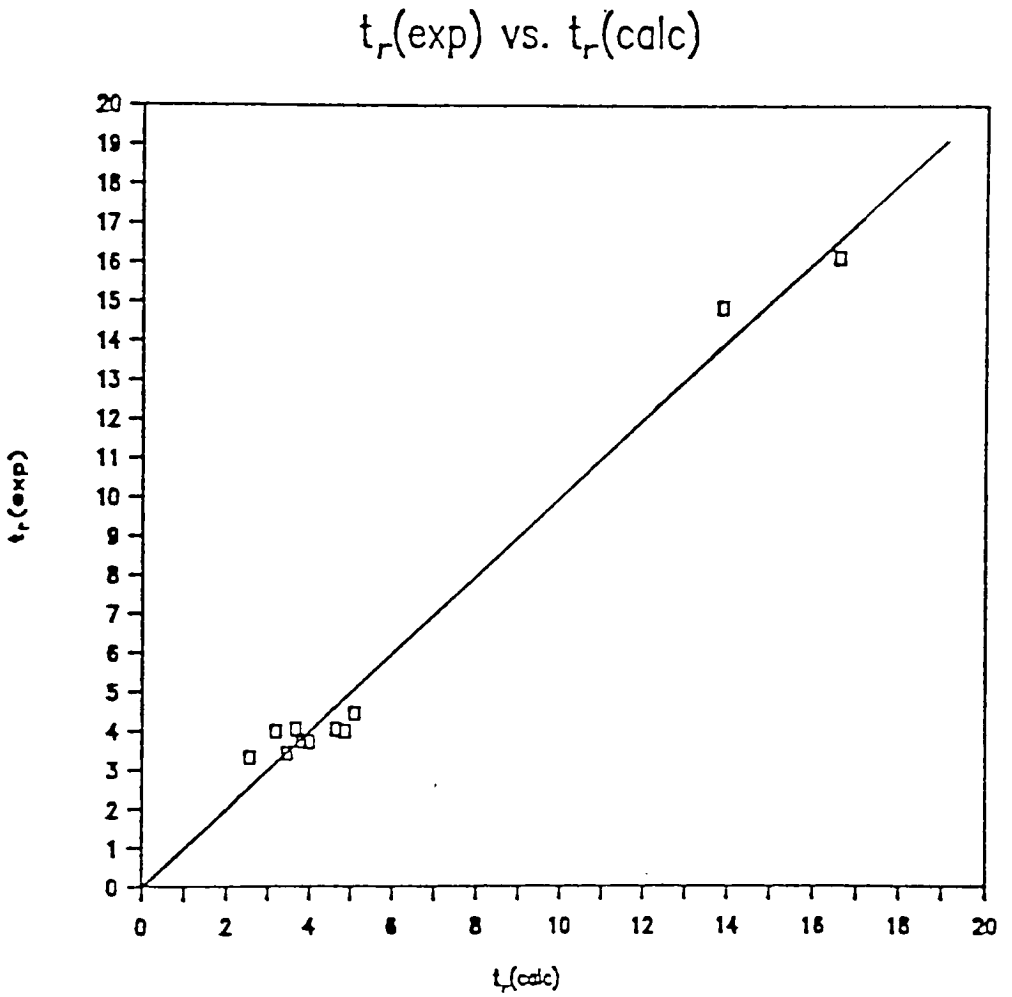

Figure 22. Plot of t_r(exp) vs. log t_r(calc) for HPLC retention data using Equation [30] to calculate predicted retention times. Solvents are those listed in Table 6.

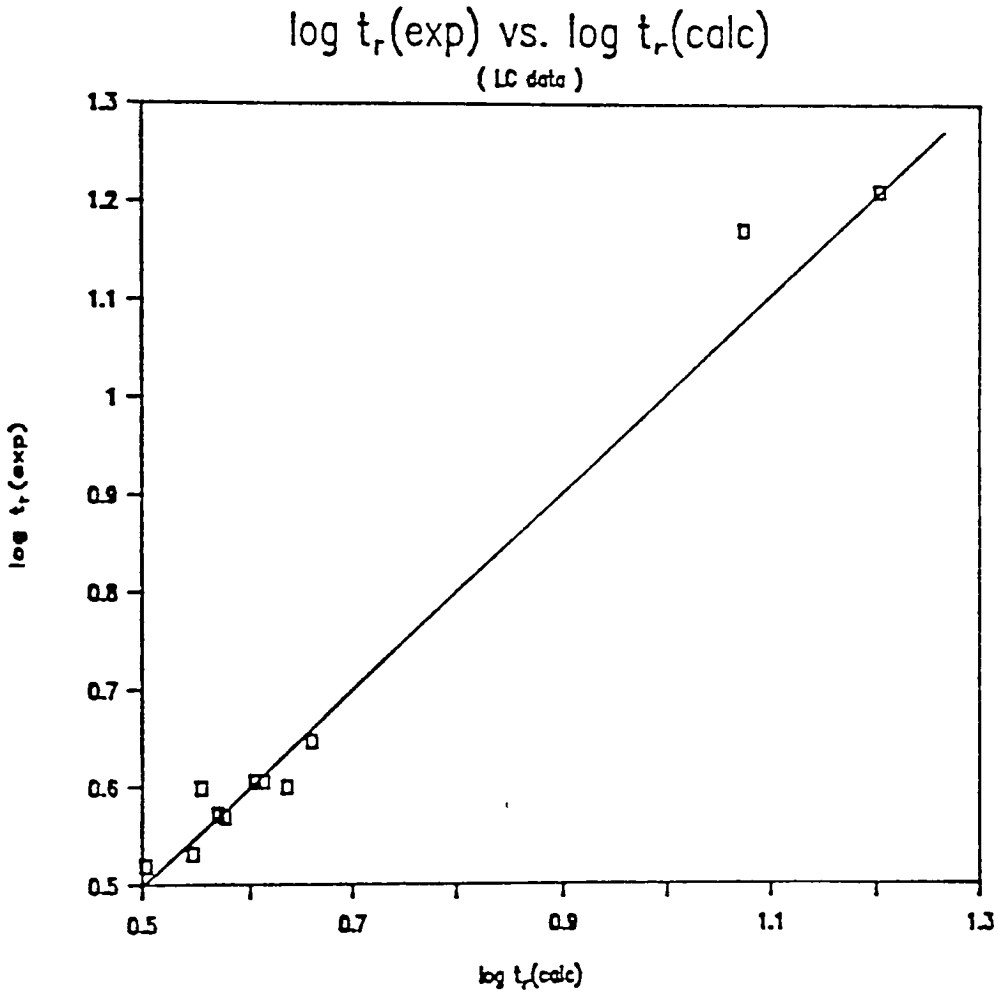

Figure 23. Plot of log t_r(exp) vs. log t_r(calc) for HPLC retention data using Equation [3] to calculate predicted retention times. Solvents are those listed in Table 6.

Individual AN and log t_r values are inserted along with average values of each from the list. b' and c' were calculated in a similar manner.

From these determinations the percent contribution, $\bar{a}$, $\bar{b}$, and $\bar{c}$ are calculated according to the following equations.

$$\bar{a} = \frac{a'}{a' + b' + c'} \qquad [33]$$

$$\bar{b} = \frac{b'}{a' + b' + c'} \qquad [34]$$

$$\bar{c} = \frac{c'}{a' + b' + c'} \qquad [35]$$

Table 7 gives a summary of these results for correlation equations [30] and [31]. "a" terms represent the AN multiplier term, "b" the DN multiplier, and "c" is the Π^* multiplier.

Table 7. AN, DN, and Π^* Contributions

Contribution Term	Equation [30] Coefficient	Equation [31] Coefficient
a	.268	.013
b	.890	.043
c	-3.22	-.089
a'	.163	.114
b'	.949	.914
c'	.318	.332
$\bar{a}$	11.4%	8.4%
$\bar{b}$	66.4%	67.2%
$\bar{c}$	22.2%	24.4%

As expected the greatest contribution to retention is due to the (b) term, which provides a quantitative measure of the solvent's donor interactions. The values of 67% indicate that most of the interactions involved in the solvent's retention are due to solvent electron donating interactions. The π^* term describes greater than 20% of the interactions involved with solvent retention. The AN interaction asserts only a minor influence on retention behavior as evidenced by the approximately 10% contribution to retention.

4.1.3 ERROR ANALYSIS AND STATISTICAL ANALYSIS

The error involved with these equations arises from the inaccuracies of the DN and AN values. The errors in these terms were determined and based on the deviations that existed in their averaging and regression limitations. DN error values are those which were calculated from the standard deviations in obtaining an average DN from individual DN values. These error estimates are given in the donor number list as shown in Table 2.

As previously mentioned, the errors in AN are : $\pm$ 2.86 for solvents other than the alcohols and chlorinated hydrocarbons, and $\pm$ 3.91 for the highly structured alcohols and chlorinated hydrocarbons. These errors are the average, absolute errors. The determination of these values is discussed in detail in Lan Evans thesis (25).

The error in the retention times is calculated via equation [36].

$$t_r\ (\text{error}) = \sqrt{(a)AN(err)^2 + (b)DN(err)^2} \qquad [36]$$

where AN(err) and DN(err) are the absolute error terms for the solvent under analysis, and (a) and (b) are their contributions in the equation used. Error in π^* are not considered due to the accuracy of determination compared to that for AN and DN.

The results of applying error analysis equation [36] to the solvents using correlation equation [27] gives the error estimate t_r(err) for each solvent's predicted retention times. All of this data is presented in Table 6.

In order to test the statistical significance of the derived equations an F-test was performed on the data from equation [36]. Along with the regression analysis of each data set an analysis of variance was done by the statistical program. Table 8 gives the ANOVA table for this.

Table 8. ANOVA Table for Equation [30]

Source of Variation	SS	Degrees of Freedom	Mean Square (MS)	F
Regression	219.4	3	73.1	126.1
Error	4.05	7	.58	
Total	223.4	10		

The value for F is calculated from MS(reg)/MS(err). From a chart of overall variance ratios it was found that in order to have an observed relationship which is statistically significant with greater than 99% probability one must have $F_{3,7}$ greater than 8.45 (26). The determined value of 126 far exceeds this minimum requirement which indicates that the observed relationship (Equation [30]) is statistically significant.

4.2 GAS CHROMATOGRAPHIC STUDIES

Gas chromatographic retention times were obtained for a wide range of solvent types. This data could not be used together with the data obtained from the LC method. The mechanism of retention in LC is very different from that in GC. The GC studies were done at a constant, controlled column temperature due to the fact that there is a strong dependency on temperature in GC retention. The solvents that were analyzed and their corresponding GC retention times are given in Table 9.

Table 9. Solvents with Gas Chromatographic Retention Times

Solvent	t_r (min)
2-propanol	0.71
ethyl acetate	0.81
ethyl formate	0.69
1-butanol	0.97
ethanol	0.58
acetone	0.89
tetrahydrofuran	0.76
DMSO	2.10
cyclopentanone	1.46
N,N-dimethylacetamide	2.23
methyl ethyl ketone	0.73
1,2-dimethoxyethane	0.86
butyl ether	2.91
diethyl ether	0.60
acetophenone	8.66
triethylamine	1.07
benzyl alcohol	8.04
cyclohexanone	3.23
tert-butanol	1.14

Simple linear regression analysis was applied to this data and, as with the preliminary LC data treatment, equations [23] and [25] were applied. A plot of (t_r/AN) vs. (DN/AN) was done and is shown with the regression analysis in Figure 24. This plot reveals poor linear relationship. Through inspection of this plot it was noticed that the points which significantly deviated from a linear relationship were, for the most part, aromatic solvent data. Therefore these values were not considered and the resulting plot (Figure 25) produced a better correlation, an 84% linear relationship. However, this is not a very reliable relationship to assume due to the presence of the dubious data point for solvent #67. By inclusion of this data point the least squares line is adjusted such that a far better correlation coefficient results. It is therefore concluded that there is no linear correlation between GC retention and only AN and DN.

The inclusion of the π^* term to the equation resulted in improved correlation with the LC study, therefore equation [28] was applied to the GC data. However, poor correlation was obtained from the application of π^*, AN, and DN solvent data to GC retention.

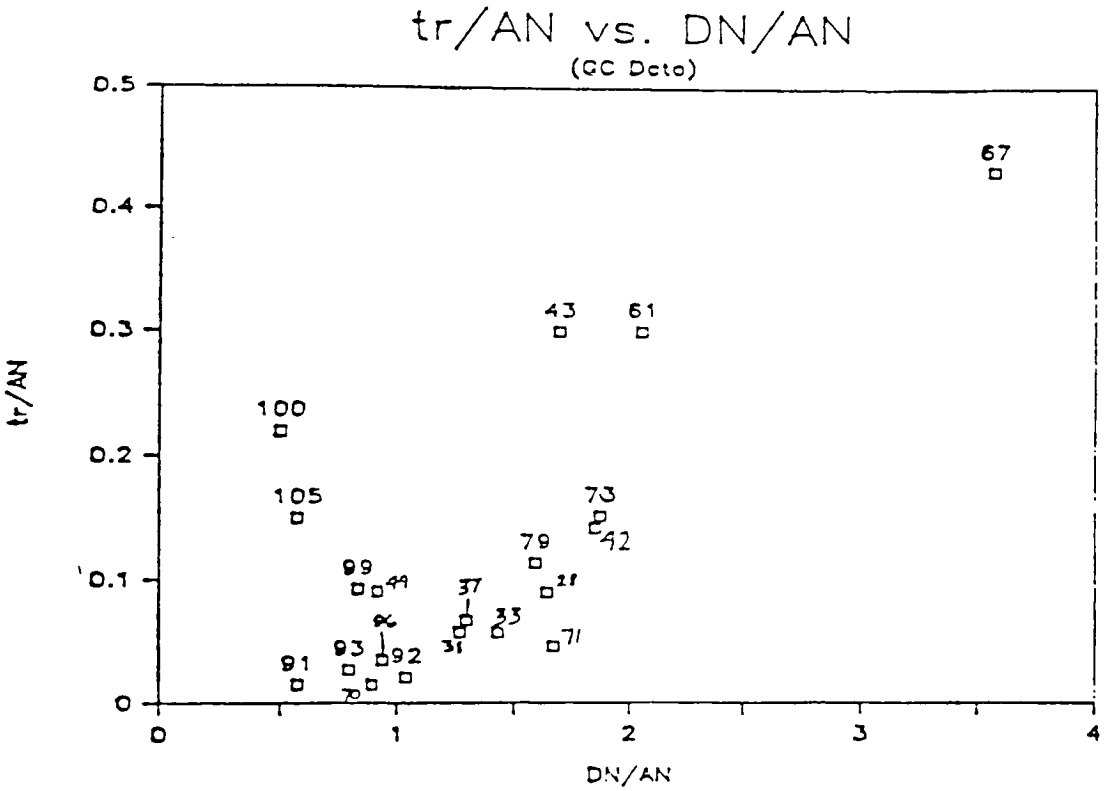

Figure 24. Plot of tr/AN vs. DN/AN using GC retention data for various solvents.

LINEAR REGRESSION ANALYSIS

REGRESSION EQUATION:

$$\frac{tr}{AN} = (.055)\frac{DN}{AN} + .074$$

SLOPE = b = .055
Y-INTERCEPT = a = .074
R-SQUARE FACTOR (% LINEARITY) = 10%

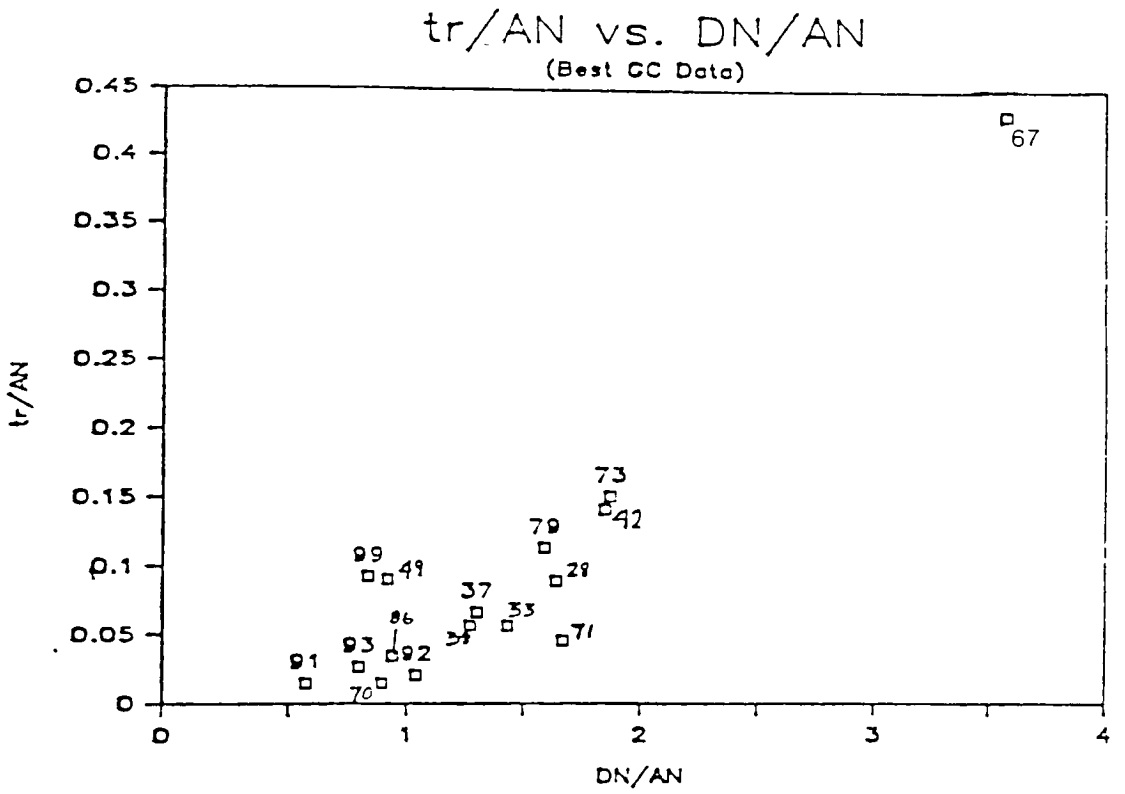

Figure 25. Plot of tr/AN vs. DN/AN using GC retention data for selected solvents.

LINEAR REGRESSION ANALYSIS

REGRESSION EQUATION:

$$\frac{tr}{AN} = (.130)\frac{DN}{AN} - 0.089$$

SLOPE = b = .130
Y-INTERCEPT = a = - 0.089
R-SQUARE FACTOR (% LINEARITY) = 84%

The relationship between boiling point and GC retention has been established. Therefore, solvent boiling point was correlated to retention times. A linear relationship was determined to exist between log t_r and the boiling point of the solvent. Using the solvents from Table 9 corelation equation [37] was determined.

$$\log t_r = .0063\ (BP) - .558 \qquad [37]$$

The correlation coefficient was determined to be .84. Retention in GC is also based upon the interactions which occur between the solvent and the stationary phase liquid. Several variations in equation [37] which included the terms : π^*, BP, DN, and AN were tested . The best correlation was achieved using boiling point, DN, and π^* data. Multiple regression analysis provided equation [38].

$$\log t = .0069(BP) - .0067(DN) - .415(\pi^*) - .242 \qquad [38]$$

The correlation coefficient for this equation is .90. Based upon a knowledge of the stationary phase the interactions which π^* and DN describe are the likely ones to occur. π^* describes the dipolar and dispersion interactions which take place in the nonpolar stationary phase. DN describes the interactions due to specific

forces of attraction which are present between solvent molecules and also between the solvent molecules and the stationary phase.

Table 10 lists the parameters of equation [38] with the experimental and predicted retention times. Figure 26 illustrates a plot of log t_r (exp) vs. log t_r(calc).

The values of DN, BP, and $\tilde{\pi}^*$ are of different magnitude, therefore partial regression coefficients were determined for the multiplication constants of BP, DN, and $\tilde{\pi}^*$, respectively represented by p', b', and c'. p', b', and c' are calculated in a manner similar to that given by equation [32]. The percent contributions, $\bar{p}$, $\bar{b}$, and $\bar{c}$ were also calculated and are given in Table 11.

Table 11. BP, DN, and $\tilde{\pi}^*$ contributions in Equation [38].

Contribution Term	Regression Coefficient
p	.0069
b	.0067
c	.415
p'	1.008
b'	.248
c'	.172
$\bar{p}$	70.58%
$\bar{b}$	12.05%
$\bar{c}$	17.37%

Table 10. Parameters (DN, π^*, BP) Used With Equation [38] To Predict GC Retention Times, t_r(calc)

SOLVENT	DN	π^*	BP	log t_r(exp) (min)	log t_r(calc) (min)	log t_r(err) (min)
2-Propanol	35.7	0.46	82	-0.149	-0.109	0.82
1-Butanol	28.8	0.46	118	-0.013	0.185	0.38
Ethanol	21.5	0.54	78	-0.240	-0.074	0.91
Benzyl Alcohol	18.4	0.58	205	0.905	0.804	0.42
t-Butanol	38.0	0.41	83	0.057	-0.097	0.82
Ethyl Acetate	14.8	0.55	77	-0.092	-0.040	0.31
Ethyl Formate	17.4	0.61	53	-0.161	-0.248	0.26
Acetone	17.2	0.71	56	-0.051	-0.267	0.12
Cyclopentanone	19.1	0.76	130	0.164	0.208	0.08
Methyl Ethyl Ketone	16.3	0.67	80	-0.137	-0.079	0.20
Acetophenone	16.2	0.50	202	0.938	0.831	0.20
Cyclohexanone	18.3	0.76	155	0.509	0.386	0.14
THF	20.7	0.58	67	-0.119	-0.161	0.12
1,2-Dimethoxyethane	8.7	0.53	85	-0.064	0.064	0.12
Butyl Ether	18.1	0.24	142	0.464	0.514	0.15
Diethyl Ether	18.5	0.27	35	-0.222	-0.238	0.11
DMSO	29.2	1.00	189	0.322	0.447	0.18
N,N-Dimethylacetamide	27.5	0.88	165	0.348	0.343	0.12
Triethylamine	45.2	0.14	89	0.029	0.008	1.18

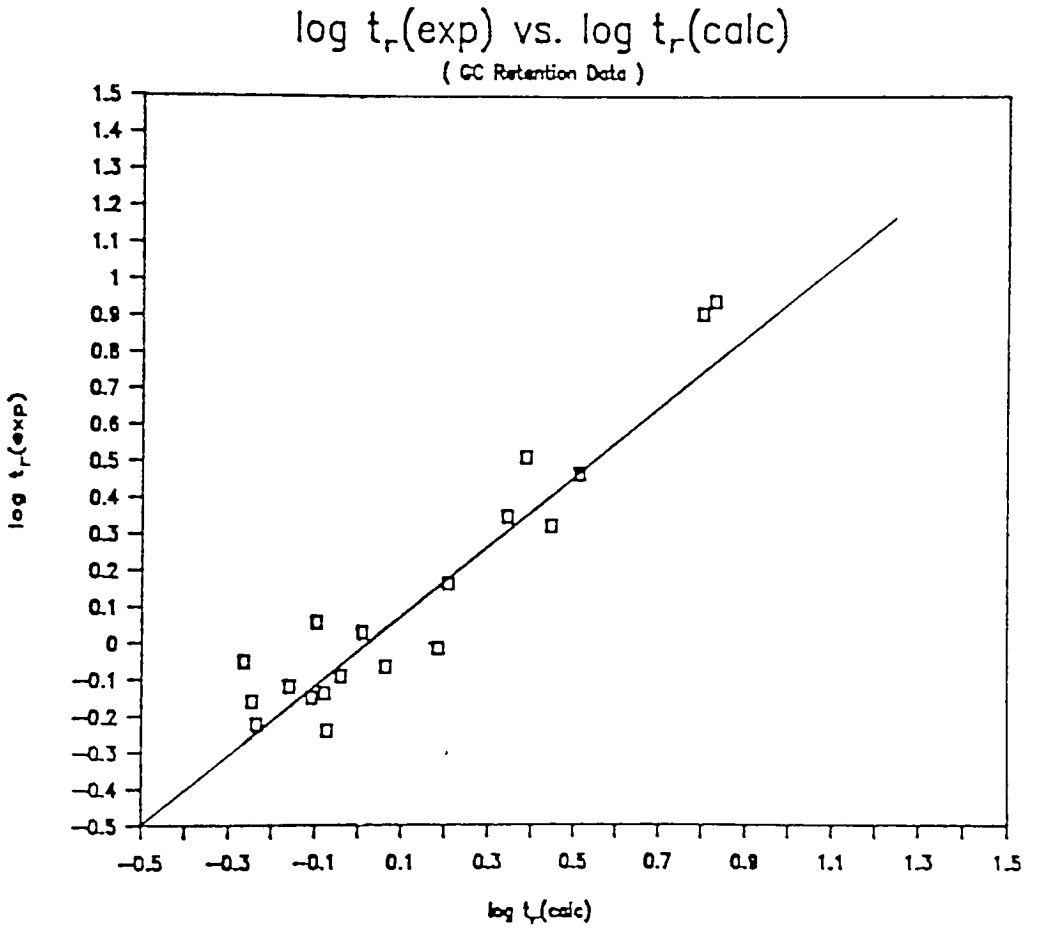

Figure 26. Plot of log t_r(exp) vs. log t_r(calc) for GC retention data using Equation [38] to calculate predicted retention times. Solvents are those listed in Table 10.

4.2.1 ERROR AND STATISTICAL ANALYSIS

The error involved with GC correlation equation [38] arises mainly from the inaccuracies in the DN values. However, due to solvent purity considerations and also to limited column thermostatting capablities an error arises from the values chosen for solvent boiling points. Therefore both BP and DN measures are considered in the error analysis of the equation. The errors in the DN values are those taken from Table 2. Boiling point error was estimated to be $1^{\circ}C$ for each solvent. The error in the predicted retention times determined by equation [38] were calculated according to equation [39].

$$\log t_r(\text{error}) = \sqrt{(p)BP(err)^2 + (b)DN(err)^2} \quad [39]$$

Error in values are not considered due to the high accuracy of determined values compared to DN and BP values. The error in the predicted retention times are given in Table 10.

To test the statistical significance of equation [38] an F-test was performed on it. Along with the regression analysis of each data set an analysis of variance was done by the Minitab statistical program. See Table 12.

Table 12. ANOVA Table for Equation [38]

Source of Variation	SS	Degrees of Freedom	Mean Square (MS)	F
Regression	2.08	3	.693	46
Error	.228	15	.015	
Total	2.03	18		

The value of F is calculated from MS(reg)/MS(err). From the chart of overall variance ratios (F distribution) it was found that in order to have an observed relationship which is statistically significant with greater than 99% probability one must have $F_{3,15}$ greater than 5.42 (26). The determined value of 46 is greater than the 99% statistically significant value of 5.42. This indicates the valid assumption of linear correlation of equation [38].

CONCLUSIONS

It was originally theorized that the chromatographic retention behavior of a solvent was dependent upon its donor and acceptor numbers. However, it appeared that this alone could not be used to accurately predict retention. Better predictions of retention in a normal phase liquid chromatographic system were obtained using correlation equations which utilize the solvent's dispersion interaction capabilities as quantified by the π^* parameter in addition to the solvent's donor and acceptor numbers.

Fairly good predictions of a solvent's gas chromatographic retention were obtained through use of a correlation equation involving the solvent's boiling point, donor number, and π^* value.

Future progress in attaining better and more universal correlation equations for a normal phase LC system would necessitate use of a more polar mobile phase capable of eluting a wider range of solvents. However, this would require some form of compensation for mobile phase interactions. Additionally, the use of directly determined values of DN and AN rather than values determined indirectly through correlations could provide improved accuracy. More reliable predictions of a solvent's gas chromatographic retention might be achieved through use of different solvent property-describing terms.

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